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LUNG FUNCTION IN COALWORKERS' PNEUMOCONIOSIS

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PREFACE

THE principal symptom of pneumoconiosis is excessive breathlessness on exertion and in 1949 Dr J C. Gilson and Dr P Hugh Jones of the Council s Pneumoconiosis Research Unit in South Wales undertook an investigation with the object of determining the precise cause of the breathlessness and relating its severity to the X ray changes in the lung which were known to occur They examined groups of normal men and representative groups of miners of comparable ages who were suffering from different degrees of pneumoconiosis as diagnosed by their chest radiographs The system used to classify the radio graphs was that originally developed by members of th Unit which divided the categories of the disease into two main forms simple and complicated pneumoconiosis having important differences both radiologically and in their natural history

Dr Gilson and Dr Hugh Jones used physiological tests to measure various aspects of lung function Some of the methods were evolved specifically for the

on exertion occurring in men with pneumoconiosis is due mainly to a reduction in the maximum ventilatory capacity of the lungs though there is also an increase in the ventilatory requirement for exercise Simple pneumoconiosis causes only slight increase in breathlessness over that which develops even in normal men as they grow older in complicated pneumocon osis on the other hand the breathlessness is often severe and its severity can be related to the rad ographic change provided that as the authors emphasize the age of the subject is taken into account A number of the observations had a more general interest in theoretical lung physiology and the interpretation and statistical treat ment of them is discussed here in detail

It is hoped that this attempt to relate disordered lung function to structural changes as demonstrated by X rays will prove useful to our understanding of the disability associated with chronic pulmonary disease and help in its prevention

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The purpose of this review is to give readers who are unfamiliar with the features of pneumoconiosis a brief description of the condition which will enable them to understand the object and plan of the main experiment described in Part II of this Report

A THE RELATION OF THE DISEASE AS IT OCCURS IN SOUTH WALES TO SILICOSIS AND TO PNEUMOCONIOSIS ELSEWHERE

THE dangerous effects of inhaling silica dust were well known before the nineteen-twenties, largely from experience in the South African gold mines, and at that time it was thought that some coalminers might develop silicosis, especially those doing 'hard heading' since this entails drilling rock. Such men were shown to have radiological signs (Tattersall, 1926, Fisher, 1935) and at post-mortem, lesions in the lung characteristic of true silicosis (Cummins, 1927). Coal-dust itself, with its small silica content, was thought to be harmless, and 'anthracosis' to have no pathological significance (Mavrogordato, 1918, 1926, Haldane, 1923). Cooke (1938), writing on silicosis in British coalfields, stated "Anthracosis denotes black lung, and as coaldust itself does not cause pneumoconiosis, even after 40 or 50 years' mining life, the term should not be used to describe a definite pathological state".

In 1931, the Welsh National Memorial Association reported a radiological investigation of coal face workers (colliers) who had done no hard heading. They showed that even these men might develop radiological changes similar to those of silicosis and that the maximum incidence was found in the anthracite area of South Wales, where many colliers were known to suffer from abnormal shortness of breath in middle and old age. Cummins and Sladden (1930) published a detailed account of the pathology of this condition and considered it to be a form of silicosis modified by the accumulation of coal-dust. However, the belief that all disabling pneumoconiosis found in coalminers was really silicosis began to be doubted, especially since Collis and Gilchrist (1928) had shown that the coaltrimmers in Cardiff docks, who are men distributing coal in the holds of ships and so are exposed only to coal-dust, might develop radiological appearances identical with those in underground coal face workers. The doubt about the effects of coal-dust itself was shown in the review of pneumoconiosis by Pancoast and Pendergrass (1931), who, referring to the disease of coalminers, stated "... while it still seems probable that silica is usually the fibrosing agent ... adherence to the general term of pneumoconiosis still seems desirable".

The significance of coal dust as a cause of pneumoconiosis remained in doubt because the Industrial Pulmonary Diseases Committee of the Medical Research Council in a report (1934) on an investigation of coaltrimmers loading anthracite at Swansea docks were unable to confirm the findings of Collis and Gilchrist. As a result, after considerable discussion at an International Conference in Geneva in 1938 (International Labour Office, 1940) it was decided "that coal dust alone does not either in animals or men, produce lesions similar to those of silicosis".

It was Gough (1940) who finally proved that coaltrimmers at Cardiff docks did develop a disabling fibrotic lesion in the lungs pathologically identical with

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that seen in coalminers, but different from the classical silicosis of the gold miner or coalminer engaged in drilling rock

The conflict of evidence about pneumoconiosis in coaltrimmers was subsequently resolved by Hart and Aslett (1942), who, by a more complete survey, confirmed the findings of Collis and Gilchrist at Cardiff and Swansea docks They stated that "whereas anthracite colliers have a generally higher incidence of pulmonary abnormality than colliers mining steam-coal, the reverse is the case *with trimmers handling the corresponding class of coal*" *This paradox* may have occurred because anthracite gives rise to little dust when shovelled in a ship in contrast to when it is mined

Thus, by 1942, there was no doubt about the effects of coal dust and in the Medical Research Council's extensive survey of pulmonary disease in South Wales coalminers, Hart and Aslett (1942) recommended (p 198) that the term 'pneumoconiosis of coalminers' should be used for the disease Today,

unique

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fields

little doubt that when coalworkers' pneumoconiosis occurs it is the same pathological process as that seen in South Wales

The descriptions given by Pancoast and Pendergrass (1925, 1926, 1931 and 1935), Bloomfield and others (1936), Sayers (1940), Flinn and others (1941) and Corcoran (1948) suggest that the same disease occurs in coalminers in the

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pneumoconiosis is similar in all coalmining areas These impressions have been strengthened by the direct comparison of chest X rays of miners in South Wales with those of other countries, Germany, France, Belgium and the United

are exposed to coal dust To quote Gough and ...

not sufficient evidence to say whether (it) is due to the chemical action of the

bituminous) workers are identical"

In some coalminers, who have done drilling and boring and been exposed to ... features of true silicosis may be combined with

and all stages between pure-

e silicosis on the other can be

found It is with the disease as seen in coalminers of South Wales that our work is concerned We must stress that the results are not necessarily applicable to true silicosis

B PNEUMOCONIOSIS IN SOUTH WALES

None of the symptoms of pneumoconiosis is specific, its diagnosis in life depends on radiological examination and an industrial history It is essentially a radiological disease accompanied by symptoms to a varying degree

Radiology

There are two main types of radiological change simple pneumoconiosis and progressive massive fibrosis (Fletcher 1948) The pathology and the results of radiological follow up studies suggest that each change represents a distinct pathological process The radiological evidence was based on the examination of many miners who had had chest radiographs taken and who either had subsequently remained at work exposed to further coal-dust inhalation or had left mining and therefore had undergone no further dust exposure (Stewart 1948 Davies Fletcher Mann and Stewart 1949) It appears that simple pneumoconiosis is the change due to the action of coal-dust which progresses only if dust exposure continues progressive massive fibrosis on the other hand is a change associated with superimposed infection probably tuberculous and once it is acquired it advances at variable rates whether dust exposure continues or not Progressive massive fibrosis is only seen radiologically in the presence of a considerable degree of simple pneumoconiosis Simple pneumoconiosis complicated by the presence of massive fibrosis is referred to as complicated pneumoconiosis The radiological appearances have been fully described (Fletcher and others 1949) and will only be summarized here

Simple Pneumoconiosis

The first radiological evidence of coal dust inhalation is the appearance of minute opacities up to 1 mm in diameter which are seen initially only in one or two rib spaces But with further dust exposure these opacities increase in

[illegible]

of resolution prevents the minute opacities themselves from being revealed though sometimes especially in elderly subjects the pattern is more reticular even with good technique Gough James and Wentworth (1949) have suggested that this altered pattern may have some pathological significance

Complicated Pneumoconiosis

The first sign of progressive massive fibrosis is a localized more homogeneous shadow on a background of simple pneumoconiosis usually appearing in the

[illegible]

not usually involve the pleura, nor is there any increase in vascular shadows converging from the suspected lesion to the hilum (Fletcher and others, 1949) Tomographs often help to establish the presence of complicated pneumoconiosis at its earliest stage The early shadow enlarges and other similar shadows may appear, each finally progresses towards the formation of large massive shadows, looking like cottonwool (Plate 7) Later the edges of the shadows gradually become more definite, sometimes with contraction in size Once the massive shadows have become more than an inch or so in diameter, cavitation may be seen within them, but this does not necessarily indicate the presence of overt tuberculosis Cavities may empty, leaving 'ring shadows', or they may later re fill The few cases of massive fibrosis where tubercle is found in the sputum have signs of toxaemia and deteriorate more rapidly

The process of expansion of the shadows followed by contraction, and cavitation when it occurs may all lead eventually to extreme distortion of the lung structure, the trachea may be markedly kinked, the hilum raised, the mediastinum displaced to one or other side, the heart shadow elongated and emphysema may appear at the lung apices and bases (Plate 8)

Pathology

Simple Pneumoconiosis

The earliest lesions are focal collections of dust, 0 4 to 4 mm in diameter, around the respiratory bronchioles (Heppleston, 1947, 1954) There is remarkably little tissue reaction to the dust in these 'coal nodules', so that although reticulin tissue develops in the deposits and later some collagen there is no dense, whorled collagen formation as in classical silicosis, and the collagenous tissue which is present is arranged radially rather than concentrically (Gough, 1940)

Focal emphysema, which is sometimes seen round silicotic nodules (Seevers, Enzer and Becker, 1938), frequently accompanies the coal nodule (Gough, 1944 1947) and four or five emphysematous spaces round a nodule may give the latter a stellate outline The severity of this focal emphysema does not necessarily correspond with the number or size of the nodules in some cases there may be numerous coal nodules with practically no emphysema, while in others the emphysema may be so extensive and close-set that the coal lesions appear diffuse and the lung section resembles a black network

[illegible] had described a medusa

At autopsy, simple pneumoconiosis gives the lung a greyish black appearance and coal dust can be seen underlying the pleura The cut surface of the lung is black from the many coal nodules which look like 'buck shot' (Cummins and

Sladden) However, the pattern of coal nodules and focal emphysema is best seen from macroscopic sections of the whole lung prepared by the technique described by Gough and Wentworth (1949), who claimed that the characteristic minute opacities seen in radiographs of men with simple pneumoconiosis [illegible]

emphysema which will be found after death, though the uncommon, marked, net like pattern seems to occur more frequently in cases showing severe focal emphysema at death It must be emphasized that the black coal, which is so obvious in the lung section, is of similar radio-translucency to the rest of the lung tissue, so that the coal nodules are seen on the radiograph only by contrast [illegible]

Complicated Pneumoconiosis

The massive lesions start as nodules showing a more extensive fibrotic process The nodules increase in size, finally forming large masses, several inches in diameter, of a hard rubbery consistency They often contain small, ill-defined caseous-like foci which may be associated with cavitation (Belt and Ferris, 1942), and an underlying tuberculous nature of these lesions has been claimed by several authors (Cummins and Sladden, 1930, Belt and Ferris, 1942, Gough, 1944, Gooding, 1946) But the finding of tubercle bacilli is not easy, the dust seems to modify the action of the tubercle and a more fibrotic lesion than is usual in tuberculosis is produced in which it is difficult to find bacteria Belt and Ferris (1942) who proposed the name 'koniophthisis' for this massive lesion when associated with tuberculosis, describe it as being " more fibrous, more chronic-looking and more widespread At the same time, it is less cellular, less caseous and seldom shows giant cell systems"

At autopsy the lung is often closely adherent to the chest wall, the pleura thickened, and bullous emphysema is common in advanced cases The black fibrous masses, seen together with the nodules of simple pneumoconiosis on the cut surface of the lung may have a soft necrotic centre and when cavitation is present a black inky fluid is found within the cavity

Heart failure is a frequent cause of death in cases of advanced complicated pneumoconiosis (Gooding, 1946) and right ventricular hypertrophy is demonstrable in spite of a generally small sized heart (Thomas, 1951)

Clinical Features

Symptoms

Shortness of breath on moderate exertion is generally the first symptom, it is rarely present at rest, though in severe cases with virtually no respiratory reserve dyspnoea comes on at the slightest increase of activity Orthopnoea is rare, and when it occurs is usually associated with signs of heart failure or severe bronchospasm

Lassitude and weakness are probably the next most common presenting features of the disease The man feels excessively tired at the end of the shift and his legs feel weak as he returns to the pit shaft or 'slant'

Cough is common but rarely precedes the breathlessness in cases of pneumoconiosis It is usually worse in the early morning, and may be dry and

unproductive, or give rise to very viscous, clear sputum, streaked with coal, which the man finds difficult to bring up In cases of complicated pneumoconiosis, however, a sudden bout of coughing may herald the onset of an attack of 'black spit', when for days or even weeks large quantities of fluid, black sputum are produced with the appearance of cavitation in the radiograph Such attacks are sometimes associated with an intercurrent respiratory infection, but often no obvious cause is found for the attack Severe haemoptysis is rare, but slight streaking of 'black-spit' with blood is common

Pain in the chest is a frequent transient complaint, but is seldom associated with pleural friction Tenderness of the intercostal muscles over the site of pain is common

Asthma like attacks, usually described as 'a feeling of tightness in the chest', are common in cases of complicated pneumoconiosis, although some degree of bronchial spasm, which may be difficult to detect clinically, may be found in all stages of the disease The presence of bronchial spasm is of importance since it affects the results of some tests of lung function

The severity of these symptoms is very variable, and, though shortness of breath is usually present to some extent, men may develop extensive radiological signs of pneumoconiosis and yet have no symptoms at all

The outstanding feature of the disease is that the breathlessness is out of proportion to the constitutional disturbance, so that apart from a limitation of their exercise tolerance, many men feel in good health

Physical Signs

No combination of physical signs is specific to the disease, and the relation of signs to radiological appearances and pathological findings shows the signs to be unreliable There is often a striking contrast between the extent of radiological consolidation and the absence of any abnormal signs on clinical examination This may be due to emphysematous lung lying between the consolidated area and the chest wall

Both loss of weight and a thin, sunken face are common, especially in cases of complicated pneumoconiosis On inspection of the chest, subclavicular ... but a barrel-shaped chest is uncommon Deviation of

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and be a sign of bronchial spasm or it may be produced by a distorted bronchial tree What contribution true bronchial spasm makes to the noisy breathing is sometimes difficult to assess, though listening with the stethoscope over the trachea (in the supra sternal notch) is often helpful, a 'wheeze', which will disappear with treatment, may then be heard, when sibili are not audible over the chest

Early recognition of cor pulmonale is important although its onset is often very difficult to diagnose A loud, often split, second heart sound in the pulmonary area conducted down the sternum is common, but a raised jugular venous pressure is less frequent Swelling of the ankles is a late sign and marked enlargement of the liver is unusual Cyanosis is practically limited to men who

breathlessness and our experience confirms the findings of Ferrer and others (1950) that it can be treated Radiology and electrocardiography help to detect its presence, the specific changes which may be seen in the electrocardiograph are described more fully later (p 88)

Although pathologically massive fibrosis appears to be a tuberculous process, the clinical features of complicated pneumoconiosis do not resemble those of tuberculosis Repeated examination of the sputum for tubercle usually gives negative results and there are few toxaemic signs, except for a raised, though very variable, blood sedimentation rate Stewart (1948) has shown that the sedimentation rate varies with the radiological progression of the massive fibrosis

Frank tuberculosis may develop in cases of coalworkers' pneumoconiosis and the patient then develops toxaemia and the prognosis is grave Mann (1951), Fletcher (1951) and Cochrane (1954) have recently published evidence on the relationship between tuberculosis and pneumoconiosis in coalminers

C RADIOLOGICAL CLASSIFICATIONS OF PNEUMOCONIOSIS

P R U Classification (1948)

The chest radiographs of all the subjects of our experiments have been classified by the system in use at the M R C Pneumoconiosis Research Unit (P R U) This system has been fully described elsewhere (Fletcher and others, 1949) It formed the basis for the latest International Classification (1950), see p 12 Only a summary, sufficient for the interpretation of the physiological results, will be given here

Principles

This classification, unlike most of those previously proposed, is based upon follow-up studies It clearly separates simple from complicated pneumoconiosis, since each is thought to be a separate pathological process It allows easy coding and is based upon illustrative films used as standards and on verbal definition, and the diagnostic errors in its use have been carefully investigated (Fletcher and Oldham, 1949, 1951)

Definitions

Simple pneumoconiosis is classified into four categories of increasing abnormality, which are given the arabic numbers 1 to 4 respectively, according to the profusion of the minute opacities, these are regarded as being the specific radiological feature of the disease Similarly, complicated pneumoconiosis is divided into four categories, given the letters A to D depending on the size and appearance of the massive shadows When one lung field differs from the other the category of the film is taken as that showing the most advanced disease

The following brief verbal definitions of these categories are based on standard films Examples of typical films together with normal ones for comparison are shown in Plates 1 9

Simple pneumoconiosis *Category* 1 The characteristic minute opacities can be seen,



completely obscured by opacities 0 5 5 mm. in diameter over all the lung fields (Plate 4)

Category 4 The lung fields have the appearance of being filled to the fullest extent by the opacities.

Complicated pneumoconiosis *Category A* Localized ambiguous shadows first appear, ambiguous in that their distinction from tuberculosis at this [illegible]

(Plate 8)

The recognition of a stage of advanced pneumoconiosis beyond that due to increase in size of the massive shadows and characterized by the anatomical distortion (category D) is peculiar to this classification We emphasize this point because our physiological findings add justification to its inclusion

Although qualitative differences* in the appearances of the pattern of the film g [illegible]
P
a
have shown them to be of no significance, either in the rate of progression of the simple pneumoconiosis or in the attack-rate of massive fibrosis

[illegible]

Coding

For brevity and convenience we use a simple system of coding, essentially the same as that described when the classification was first published

The main features of any film are described in the following manner first, the arabic number appropriate to the category of simple pneumoconiosis is given, then a letter represents the category of complicated pneumoconiosis, or a dash signifies that only simple pneumoconiosis is present Two arabic numbers follow, separated by an oblique stroke, these indicate the number of anterior rib spaces in the right and left lung fields respectively over which the massive fibrosis extends, (these numbers are replaced by dashes when there is no massive fibrosis) In some films of advanced complicated pneumoconiosis, the underlying degree of simple pneumoconiosis cannot be classified, in which case a question mark replaces the first number in the code

Thus, a film showing only simple pneumoconiosis of category 2 would be represented as 2- /-, while a film of complicated pneumoconiosis showing category B massive fibrosis overlying a category 3 simple pneumoconiosis by three rib spaces on the right and two on the left would be 3B3/2 Normal films

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* [illegible]

been described

[illegible]

a cross within the 0, thus ⊕

Other Classifications

We refer to other systems of classifying the X ray appearances of pneumoconiosis, for in nearly all other studies of lung function with which we are concerned, the subjects have either had silicosis or, where they had coalworkers' pneumoconiosis, the distinction between this disease and true silicosis has not been drawn Some of these other systems of classification will now be summarized in chronological order

International (1930)

[illegible] sil [illegible] In [illegible] th [illegible] Labour Office, 1930)

South African

[illegible]

In addition, a group of silicosis with tuberculosis was recognized

American

Pancoast and Pendergrass (1931) classified silicosis in three stages Later an authoritative committee (Pancoast *et al*, 1935) modified the South African system so that it would cover the radiological appearances of silicosis as it develops in a variety of industries They used three groups covering nine stages of the disease

The U S Public Health Service (1935) used another classification in which the radiological changes were divided into four phases

French

The French abandoned the three stage classification of the 1930 International Conference in favour of a system, introduced by Eck and Hanaut (1944) more generally applicable to most forms of pneumoconiosis This system sometimes with minor modifications, was in general use in France until the new Anglo-French system (Cochrane, Davies and Fletcher, 1951) was agreed This is essentially the same as the International Classification (1950)

British

The International Classification of 1930 was modified by Sutherland and Bryson (1929) and used officially by the Medical Board for purposes of compensation When, however, Hart and Aslett (1942) did their survey in the mines of South Wales they found certain differences from the X-ray changes described for classical silicosis They developed their own classification in which a film

TABLE

Radiological classifications

	International ILO 1950 Anglo-German-French 1951–2*	British: PRU 1948	British: Hart and Aslett 1942	British: Hart and Aslett 1942	British: Silicosis Boards pre-1943	German (Swiss)	French (Belgian)
	O (X)	O	*Normal*			O	N (P)
Simple Discrete Pneumoconiosis	1	1				O-I	F Images lineares
	2 (P) (M) (N)	2	*Reticulation*			I	M Micro nodulaire
	3 (P) (M) (N)	3 4	*Nodulation*	*Consolidation*	*Silicosis* I		N Nodulaire
Complicated Massive Pneumoconiosis (P M F)	A	A	*Coalescent nodulation and multiple fluffy shadows*		*Silicosis* II	II	T Condensation
	B	B					
	C	C	*Massive shadows*		*Silicosis* III	III	Pseudo-tumorale
	D	D					

* [illegible] M) refer to qualitative differences within the categories of simple pneumo[illegible] were omitted from the P R U [illegible] to be of no practical

1

of pneumoconiosis

American		South African (Miners Phthisis Medical Bureau) 1936	International I.L.O 1930
Pancoast and Pendergrass 1931	U S Public Health Service 1935		
First stage	*Linear phase* 1st and 2nd degree Exaggeration of lung markings	*Simple and infective* 1 Healthy lung 2 Moderate increased linear striation	
Second stage	*Granular phase* 1st degree 2nd degree *Nodular phase* 1st up to 1 mm 2nd over 1 mm Silicosis I and II according to symptoms	3 Marked increased linear striation 4 General arborisation 5, 6, 7, 8 } Increased size of mottling	*Silicosis I* Symptoms slight or absent *Silicosis II* Definite impairment of function
Third stage	*Coalescent nodules and conglomerate shadows* = Silicosis II and III according to symptoms	*Silicosis with tuberculosis*	*Silicosis III* Marked impairment of function

radiograph They concluded that in these men the total capacity of the lung was reduced, *due to a small vital* capacity, in contrast to cases of emphysema who had a normal total volume The residual volume, expressed as a percentage of the total lung volume, was increased in two cases but these were *also* the oldest subjects

Hurtado *et al* (1935) extended their series to 58 cases of pulmonary fibrosis, all but 4 having an industrial history of exposure to siliceous dust The subjects were divided into six groups on the appearance of the radiograph, and the authors concluded "a definite correlation exists between the average observed values for the pulmonary capacity of the various groups and the nature and extent of the pulmonary lesion seen in the roentgenographic film" *

Other investigations in this same series showed an increased ratio for "area of the chest on inspiration to that on expiration" in all groups except the first, *a nearly normal respiratory dead space calculated from the Bohr formulae* using carbon dioxide and oxygen, and a good relation between residual air as a percentage of total lung volume and the clinical assessment of dyspnoea from the clinical history The possible influence of age on the results is not commented upon

These results bring out a point often overlooked when considering the significance of a raised residual volume as a percentage of total lung volume, namely that this can arise either from a reduced total lung volume or an absolute increase of residual volume

Kaltreider and McCann (1937) used a bicycle ergometer to study the effect of various grades of exercise on ventilation, on the ventilation equivalent for oxygen and on the arterial blood oxygen saturation in 11 cases of pulmonary fibrosis of industrial origin They estimated the 'pulmonary reserve' both as total ventilation/vital capacity and as (minute ventilation/maximum minute ventilation) × 100 The maximum minute ventilation for the second ratio was obtained under maximal exercise conditions and presumably was less than the maximum breathing capacity The second ratio was the better index of dyspnoea The oxygen saturation of arterial blood rose during exercise in a majority of cases Since this study was limited to 11 subjects, it was not possible to relate [illegible] category to the ventilation indices

[illegible] udy of 2711 anthracite workers used [illegible] rker was subject to a uniform test in which one foot was placed on a chair and the body raised to an erect position 25 times in 30 seconds" Their results showed a definite relation between dyspnoea and the stage of silicosis The exercise was not standardized for weight and the results depended on a subjective assessment *of dyspnoea It is of* interest that they observed a marked impairment of diaphragm movement in *silicosis*

Seevers, Enzer and Becker (1938) used the effect of a decreased concentration [illegible] the inspirate as a test of cardiopulmonary function in 139 men [illegible] three [illegible] art [illegible] on

* [illegible] (1939) in reviewing this and previous papers by the same [illegible]

dioxide content as indices They did not find a close relation between the test results and the degree of radiological abnormality, and they concluded that anoxaemia was not the cause of dyspnoea in pulmonary fibrosis They were impressed by the importance of age, since in all groups of fibrosis the circulatory response was poorest in the oldest subjects

In the reports of the third and fourth Symposia on Silicosis at Saranac Laboratory, McCann (1937, 1939) stressed the interrelation of cardiovascular and pulmonary failure He reported that the presence of cardiac failure in

and he suggested that this condition might be commoner in miners with anthraco-silicosis because they lived longer than men with silicosis, many of whom developed tuberculosis and so died young He concluded from a small series of 16 cases of advanced fibrosis, that right axis deviation high residual air percentage of total lung volume and desaturation of the blood at rest, tended to occur together, and that right heart strain appeared subsequent to a rise in the percentage of residual air Examination of the pulmonary circulation time

capacity, was the cause of the dyspnoea

During the discussion of his paper at the fourth Symposium on Silicosis, McCann said 'he did not know whether there was any physiological reason for dyspnoea in uncomplicated cases of silicosis' and also that he thought cases of dyspnoea without evidence of radiological change must be due to causes outside the lung It is thus quite clear that there were many gaps in the knowledge of the relationship of pulmonary function to radiological stage in pneumoconiosis at the beginning of the war in 1939

Wright (1942) reported a very careful comparison of 48 cases of silicosis and 21 control subjects The controls were selected from miners and surface workers without radiological evidence of disease and were of the same age as the men with silicosis (mean age 46) None of the subjects complained of dyspnoea The miners with silicosis were divided into five radiological categories No difference was found between the normal and abnormal groups in vital capacity, mid-capacity (see Table 5, p 35), residual air percentage of total lung volume, or in the percentage of nitrogen in the alveolar sample after breathing oxygen for 7 minutes, or in the oxygen consumption or the ventilation for a standard amount of work during a strenuous exercise test In the maximum breathing capacity a difference was observed the ventilatory capacity in the group with silicosis but without conglomerate shadows was slightly reduced but not sufficiently to prevent them working Later Wright (1946) affirmed his belief 'that simple discrete nodular silicosis is with rare exceptions entirely compatible with a working capacity adequate to allow full employment" He emphasized the wide variation shown by normal subjects and commented that "even men with a conglomerate silicosis often have a useful working capacity and benefit mentally and physically by continued employment" However, he stated (1949) that radiographs were of some use for assessing lung function, "because if the roentgenographic evidences of anatomic damage are absent one must accept with caution the claimant's history that he has severe respiratory disability

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Hurtado *et al* (1935) extended their series to 58 cases of pulmonary fibrosis all but 4 having an industrial history of exposure to siliceous dust The subjects were divided into six groups on the appearance of the radiograph and the authors concluded "a definite correlation exists between the average observed values for the pulmonary capacity of the various groups and the nature and extent of the pulmonary lesion seen in the roentgenographic film" *

Other investigations in this same series showed an increased ratio for "area of the chest on inspiration to that on expiration' in all groups except the first, a nearly normal respiratory dead space, calculated from the Bohr formulae using carbon dioxide and oxygen, and a good relation between residual air as a percentage of total lung volume and the clinical assessment of dyspnoea from the clinical history The possible influence of age on the results is not commented upon

These results bring out a point often overlooked when considering the significance of a raised residual volume as a percentage of total lung volume, namely that this can arise either from a reduced total lung volume or an absolute increase of residual volume

Kaltreider and McCann (1937) used a bicycle ergometer to study the effect of various grades of exercise on ventilation, on the ventilation equivalent for oxygen and on the arterial blood oxygen saturation in 11 cases of pulmonary fibrosis of industrial origin They estimated the 'pulmonary reserve' both as total ventilation/vital capacity and as (minute ventilation/maximum minute ventilation) × 100 The maximum minute ventilation for the second ratio was obtained under maximal exercise conditions and presumably was less than the maximum breathing capacity The second ratio was the better index of dyspnoea The oxygen saturation of arterial blood rose during exercise in a majority of cases Since this study was limited to 11 subjects, it was not possible to relate the radiological category to the ventilation indices

Bloomfield and others (1936) in their study of 2711 anthracite workers used a 'clinical exercise test in which "each worker was subject to a uniform test in which one foot was placed on a chair and the body raised to an erect position 25 times in 30 seconds" Their results showed a definite relation between dyspnoea and the stage of silicosis The exercise was not standardized for weight and the results depended on a subjective assessment of dyspnoea It is of interest that they observed a marked impairment of diaphragm movement in silicosis

Seevers, Enzer and Becker (1938) used the effect of a decreased concentration of oxygen in the inspirate as a test of cardiopulmonary function in 139 men, both normal and with various stages of pneumoconiosis classified into three groups of increasing radiological abnormality They used the change in heart rate, blood pressure, minute volume and venous blood oxygen and -carbon

* Baldwin Cournand and Richards (1949a) in reviewing this and previous papers by the same

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In the reports of the third and fourth Symposia on Silicosis at Saranac Laboratory, McCann (1937, 1939) stressed the interrelation of cardiovascular and pulmonary failure He reported that the presence of cardiac failure in

and he suggested that this condition might be commoner in miners with anthracosilicosis because they lived longer than men with silicosis, many of whom developed tuberculosis and so died young He concluded, from a small series of 16 cases of advanced fibrosis, that right axis deviation, high residual air percentage of total lung volume and desaturation of the blood at rest, tended

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In the studies of ventilation the only group to show striking changes in the resting values were those men with severe dyspnoea in the third stage in which the respiratory rate was raised and the tidal volume reduced There was no alteration of the ventilation equivalent for oxygen, even in the worst cases Polycythaemia was not present and the resting oxygen saturation was above 90 per cent in all subjects, with a mean saturation of 94 per cent even in stage III

Bruce's monograph contains a full review of the literature and the results are critically analysed It is the fullest account so far published of the relation of radiological disease stage to lung function In the statistical treatment the groups are related in pairs, a method which does not take into account the additional information that in nearly all test results there is a uniform trend from the first to the third stage of silicosis, thus the relation between radiological stage and

[illegible]

conclusions

Germany

Tamman and Bruns (1923), using a hydrogen dilution method, measured the total lung volume in a group of 30 miners working in a potassium mine at a depth of 808 metres Estimates were made before, during and after working, and also after going down and up again without working There was an increase of residual air and functional residual air which was attributed to the effect of pressure, but the authors do not appear to have completely eliminated the possible effects of exercise and an increase of bronchial spasm due to the mine atmosphere The paper was ahead of its time in emphasizing the effect of age on residual air percentage of total lung volume, the value of which was highest in the older group, some of whom had bronchitis The authors comment that, although some subjects had an increased residual air percentage of total lung volume, they had not got clinical emphysema

Böhme (1938, 1939) estimated the exercise ventilation in young normal men and found that it increased with age In 12 subjects with silicosis, who were selected partly on account of their ability to give reproducible results, it was observed that the respiratory rate was over 22 at rest and that it increased to a greater extent on exercise than it did in normal subjects, their ventilation after exercise also continued at a raised level for a longer period Some subjects had a 50 per cent reduction of maximum breathing capacity Whereas in young normal subjects the maximum breathing capacity increased with increasing breathing rate, this was not so in the older subjects or those with silicosis The author also pointed out the functional inefficiency of very high rates of breathing because the associated small tidal volume becomes nearly the same size as the [illegible]

2 cases of silicosis to illustrate their methods They used both spirometric examinations and graded exercise tests on a bicycle ergometer In silicosis they found a reduced maximum breathing capacity (accompanied by a rise of the expiratory level on the spirogram) and an increased ventilation on light exercise, disturbances which were thought to indicate a mechanical derangement of function with little disturbance of gas exchange There was no increased oxygen

Pelnar (1949) proposed a new test of pulmonary function which aimed at overcoming errors caused by hyperventilation, the ventilation equivalents for

These results from the United States added greatly to our knowledge of methods for investigating lung function, but the exact nature of the disability in pneumoconiosis and its relation to the radiological stage of the disease is not clear from them

Scandinavia

Possibly because there are no large mining communities in Scandinavia the study of lung function in pneumoconiosis started later there than in other countries in Europe or in the United States

Roelsen and Bay (1940) could find only one previous reference in the Scandinavian literature—that of Stub Christiansen in Denmark, who found that the vital capacity was generally reduced in silicosis but not to a marked

tion There was agreement between the clinical, roentgenological pictures and the physiological results in two thirds of the cases, but there were some notable discrepancies

Roelsen and Eskildsen (1941) extended the tests to include the effects of exercise Most of the advanced cases showed a marked increase of ventilation, their 'oxygen debt' was increased, and many were unable to complete the test

Bruce (1942), in a monograph covering many aspects of silicosis in Sweden, included the results of physiological investigations He examined a total of 173 cases composed of men referred to hospital and others whose silicosis was detected in a radiological survey of an industrial population Each of the three stages of silicosis was subdivided for the purpose of analysis into men with three grades of dyspnoea (1) with no symptoms, (2) capable of work but short of breath, (3) incapable of work on account of shortness of breath Only in the third radiological stage was each grade of disability adequately represented

Height and weight, chest expansion, and heart volume estimated radiographically, were not appreciably different in the three stages The average total lung volume decreased uniformly with disease stage and also, within each stage, with the grade of dyspnoea This reduction was principally due to a fall in complementary air The values for residual air percentage were lower than those

constant, whereas a rapidly advancing lesion reduced the vital capacity
the residual air

capacity in the later stages and occasionally in the first stage They emphasized the importance of age in affecting both measurements They considered functional tests, especially those requiring exercise, to be useful in cases where silicosis was complicated by other diseases

Michaud (1945), commenting on the results obtained by Jequier-Doge, stressed the variability of the results in individual subjects and pointed out that there was often a striking contrast between the radiological stage and the pulmonary function tests

Loh (1947) [illegible]

[illegible] of papers describing the results of using a comprehensive series of lung-function tests, including calculation of functional dead space and indices of oxygen uptake [illegible]

Spa[illegible] (Rossier, 1945)

In 1947, Rossier, Bucher and Wiesinger reviewed their observations on functional tests in 137 cases of *silicosis* at rest seen over a period of 9 years. All the men were attending hospital or applying for compensation under insurance schemes They stressed that there are many cases where the radiological appearance gives a poor indication of pulmonary function and as a result they preferred to classify their cases on the basis of functional tests and not radiographs However, they stated that in large groups there was a relation between radiological stage and pulmonar[illegible]

Th[illegible] with [illegible] breat[illegible] adre[illegible] No[illegible] vent[illegible]ation, used as a measure of [illegible] dead-space increased with the [illegible] the oxyger[illegible]

In a late[illegible] tests on 1[illegible] circuit ap[illegible] breathing [illegible] the subjects were not al[illegible] comparable to that used [illegible] that the exercise oxyge[illegible] the most use[illegible]

These [illegible] lung funct[illegible] that no allowance [illegible]s of severe[illegible] true relation be[illegible]

Mieville (19[illegible]

uptake on breathing oxygen in place of air, that is to say, there was no oxygen debt at rest.

Gaubatz (1940) applied a combination of tests to 12 cases coming for compensation assessment for silicosis His cases were divided into three groups, but these were too small for rela

were chosen as representative of

The tests consisted of spirometr

severity on an ergometer In addition to oxygen consumption, the blood pressure, pulse-rate and a continuous electrocardiogram were recorded The results in general supported the conclusions of Bohme, and of Rothkopf and Linxweiler, that the main lesion in silicosis is a reduction in the ventilatory capacity

Zorn (1940) investigated lung and circulatory function in miners, using the usual German techniques of spirometry and ergometry at a series of increasing work-levels He agreed with the views of Reichmann that function is not closely related to radiological appearance His 106 cases of silicosis were divided into three groups corresponding with the 1930 International Classification (see Table 1, pp 10, 11) In the first group, the maximum breathing capacity and

was limited to about 200 watts on the bicycle ergometer, but the author comments that as miners do not have to maintain such high levels of activity as this at work they may still be able to do their job although their maximum is below normal Men were thought to be seriously incapacitated if the arterial oxygen saturation decreased after 3 minutes' exercise at 150 watts In the third group, which was divided into those with apical, middle and lower zone massive shadows, all had a severe limitation of exercise capacity There was a tendency for disability to be greater, the lower the position of the massive shadows The importance of emphysema in the severe cases and the complicating effects of cardiac insufficiency were emphasized

Later, Zorn (1950), studying a group of 159 cases, found no significant increase of resting minute volume in any grade of silicosis nor a change in ventilation equivalent for oxygen, and he was thus unable to confirm the findings of Bohme, and of Rossier in Switzerland He found a marked change of maximum breathing capacity with disease stage Inhalation of adrenaline produced only a small rise of vital capacity and maximum breathing capacity The author concluded that in Ruhr miners 'spastic bronchitis' is not very common and that the reduction of maximum breathing capacity in severe silicosis is not principally due to spasm

Switzerland

were compared with those without A group selected in this way is not well suited to reveal the relationship of radiographic disease stage to function, so that the findings have to be interpreted with caution These authors observed a reduction of vital capacity but a more marked reduction of maximum breathing

* International Classification (1930), Table 1, pp 10 11

literature dealing with simple methods of testing lung function and their interpretation in cases of silicosis Gautier (1945), Croizier (1947), Mottard and [illegible]

[illegible]

general the methods of selection of subjects means that the results are unsuitable for relating the degree of disability and radiological change

Other Countries

In Czechoslovakia an account of a symposium on lung function in silicosis has been published* Vokac (1950) used a group of normal subjects without a history of dust exposure as controls, but also included a group of miners without radiological evidence of silicosis There was a statistically significant reduction of maximum breathing capacity but not of vital capacity in the group of miners without evidence of silicosis compared with the normal controls, but there was no statistically significant difference between miners with simple silicosis† and miners without radiological evidence of disease Miners with complicated silicosis showed a statistically significant reduction of maximum breathing capacity and vital capacity compared with the other groups of miners The effect of age was well controlled This paper brings out the difficulty of relating radiological disease stage to disability when compensation is at stake, and the authors concluded that the maximum breathing capacity is not a suitable test

Kadlec and Vyskocil (1950), appreciating the difficulties of getting good co-operation in measuring the maximum breathing capacity in compensation cases, investigated the characteristics of a series of single fast expirations into a low resistance recording spirometer An empirical formula, which was a [illegible]

[illegible]

graphic evidence, into four groups group 1 had some evidence of pneumo*coniosis but less than reticulation or nodulation, group 2 had reticulation*, group 3 had 'ordinary' silicosis and group 4 had silico-tuberculosis The average ventilation index fell as disease stage increased, and there were statistically significant differences between the normals and group 1, and also between groups 2 and 3, and groups 3 and 4 The scatter about the mean for this test was less in each group than for the maximum breathing capacity which did not show significant differences between the groups

These authors also investigated a group of 97 cement workers These were div[illegible]
on [illegible]
bet [illegible]
single fast expiration is a useful alternative to the maximum breathing capacity as a means of measuring ventilatory capacity, it is easy to perform and has good power of discrimination The tests on cement workers do not prove that respiratory disability is produced by cement dust, but indicate the need for functional assessment in a dusty occupation which has been shown to produce no gross radiological abnormality

* See under Vokac (1950) We are grateful to Dr W Grosz for translating these papers

† The classification used was derived from the P R U system

abnormal from the results of this test, but the author points out that even a normal test response does not prove that the individual will not be unduly dyspnoeic on exercise

France and Belgium

Roche and Thivollet (1949) reported the results of a detailed investigation

and chest expansion showed no marked differences between men in the early stages, whereas in the third stage about half the subjects were definitely abnormal The vital capacity and the maximum breathing capacity were reduced progressively with increasing severity of disease

The volume of gas expelled in one second was recorded by a spirometer, and their results support the observations by Tiffeneau, Bousser and Drutel (1949) Kennedy (1950), Kadlec and Vyskocil (1950) and Gaensler (1951) that this test may be a useful and easy way of measuring a ventilatory function closely related to the maximum breathing capacity Other tests used were *maximum ventilation when stimulated by carbon dioxide during a period* of rebreathing into a spirometer, the pneumotachogram and a method of measuring the 'work of the lung' The last test appears to be considerably dependent on the type of spirometer used for the measurement

Ruyssen (1951) gave the results on 140 subjects examined for diagnosis and assessment of compensation Vital capacity and the maximum breathing capacity were calculated from a single forced expiration by the method suggested by Tiffeneau and others (1949) A table in the paper showed the age radiological

Guillet (1951), in a

silicosis cases, gave the results on 118 coalminers, some of whom were examined

The subjects were divided

cording to the 1930 Inter-

maximum breathing capacity was measured both directly with a spirometer and also calculated by the Tiffeneau method, which gave values systematically greater than the direct method, this difference was thought to result from

breathing capacity

Lavenne and Belayew (1953) studied 250 working miners, including 32 with complicated pneumoconiosis, but found no relation between the maximum breathing capacity or vital capacity and the radiological severity of the disease This unusual result they ascribed to the effects of selection, the more disabled miners having left the mines

In addition to these detailed results which have been used to relate tests to radiological appearance, there have been a number of reviews in the French

supply might all be disturbed There is no precise agreement about the nature of the functional disturbance in the lungs in pneumoconiosis

values all showed the same downward trend In the third stage there is a marked reduction of vital capacity with the residual volume either normal or slightly increased so that the residual air percentage of total lung volume is raised This value has been used as a measure of the degree of emphysema in pneumoconiosis without regard to whether it was caused by a reduction of the vital capacity and a normal absolute residual air, or to an absolute increase of residual air The effect of age on this ratio, first emphasized by Tamman and Bruns (1923), has often been forgotten

The most striking change found in pneumoconiosis has been reduction of maximum ventilatory capacity The measurement of this function by the voluntary maximum breathing capacity test has shown a bigger reduction with increasing disease than any other single test The maximum breathing capacity increases after adrenaline in all stages of disease suggesting that at least part of the reduction results from bronchial spasm Several observers have found this test unsuitable when compensation issues were at stake, in these circumstances a promising alternative index seems to be the maximum volume of air which can be expelled in the first 0 75–1 0 second during an estimation of the vital capacity

There is disagreement on whether the resting ventilation is increased or not, but there is a preponderance of evidence in favour of an increase of respiratory rate at rest in the later stages of the disease Many observers have stressed the usefulness of exercise tests to uncover deficiencies not apparent at rest In Europe, the exercise has usually been on a bicycle ergometer, and the work level increased by stages until the subject could do no more The indices of impairment are then the maximum load achieved and the ventilation or

test In America a stepping test has often been used with submaximal loads, and has not been standardized for weight so that the work done depends partly on the build of the subject The exercise ventilation (but not always at a 'steady state) is expressed as a ratio of the maximum breathing capacity to give an index of dyspnoea However, an index of this type has not been related to the stage of pneumoconiosis in any large group of subjects

There is universal agreement that arterial oxygen saturation at rest is not altered in the first two stages but is reduced below 90 per cent in the third Polycythaemia is rare On exercise there is a lowering of oxygen saturation in some cases and a rise in others The change has not been closely studied in relation to radiological appearances In German reports it is usually assumed that the limit of exercise tolerance is set by the oxygen debt,

* International Class fication (1930)

Other papers ...

func

with

exercise assessment, and David (1950) estimated the oxygen saturation of arterialized ear capillary blood by the Roughton Scholander micro method Pelnar (1950) described his method (p 18) for the simultaneous estimation of ventilation equivalents for oxygen and carbon dioxide, and concluded the best measure of pulmonary function by this method was obtained by adding the sum of the resting and maximum equivalents, equivalents during the recovery period were very variable

In Russia, vital capacity measurements on a group of 431 cases of silicosis and on 96 normal control cases were made by Evgenova (1948) The average vital capacity decreased with increasing silicosis, though those in the first stage had a higher average capacity than the normal men The authors attributed this increase to the early development of compensatory emphysema in the first stage though the difference of the means was clearly not significant Exercise tests were also used but only respiratory rate and pulse rate were recorded

In Italy, Caccuri and Di Lauro (1949) examined a small group of 12 cases of silicosis by spirometry The effects of raising the oxygen concentration to 50 per cent and reducing it to the lowest tolerable limit were investigated, the results

subjects were examined

Parmeggiani (1950a, b) examined a group of 424 patients with silicosis attending a hospital clinic He reported a decrease of the average vital capacity with increasing silicosis, but considered it better related to the degree of emphysema than the fibrosis, though he does not state how the emphysema was measured

Conclusions

One of the most striking features of previous work comparing lung function with radiological appearance is the lack of balance between the care with which

included irrespective of size It is probably no accident that McCann *et al* (1934), who divided their radiographs into six groups, have reported a closer relationship between function and the radiograph than the majority of workers, and that Motley *et al* (1949) found no relationship when studying a group in which two thirds of the cases were in the last group Ruyssen (1951) and Guillet (1951) on the other hand used the classification of Eck and Hanaut but found that the number of possible groups was too large to allow satisfactory analysis It seems reasonable to conclude that one cause of the failure to relate function to radiographic appearance may have been the lack of interest among physiologists in applying to the reading of the radiographs the same standards they required before accepting the results of functional tests

The tests of function have varied from the simple exercise test used by Hart and Aslett (1942) to the complex indirect methods of measuring ventilation perfusion ratios used by Rossier, Bucher and Wiesinger (1947) and Motley, Gordon, Lang and Theodos (1950) As Lang (1947) noted, increasing the complexity of the tests has not in general improved the relationship between the

radiological appearance and the physiological estimate, in fact the reverse is true This might be expected because the more complex tests are more specific to a single aspect of the lung function, and in pneumoconiosis the morbid anatomy suggests that the lung volume, ventilation, gas mixing and blood supply might all be disturbed There is no precise agreement about the nature of the functional disturbance in the lungs in pneumoconiosis.

When there have been approximately equal numbers in each of three radiological stages,* nearly all observers have reported a progressive decrease in the total lung volume with disease The reduction in vital capacity in the first two stages has never been shown to be statistically significant, but the average values all showed the same downward trend In the third stage there is a marked reduction of vital capacity with the residual volume either normal or slightly increased, so that the residual air percentage of total lung volume is raised This value has been used as a measure of the degree of emphysema in pneumoconiosis without regard to whether it was caused by a reduction of the vital capacity and a normal absolute residual air, or to an absolute increase of residual air The effect of age on this ratio, first emphasized by Tamman and Bruns (1923), has often been forgotten

The most striking change found in pneumoconiosis has been reduction of maximum ventilatory capacity The measurement of this function by the voluntary maximum breathing capacity test has shown a bigger reduction with increasing disease than any other single test The maximum breathing capacity increases after adrenaline in all stages of disease suggesting that at least part of the reduction results from bronchial spasm Several observers have found this test unsuitable when compensation issues were at stake, in these circumstances a promising alternative index seems to be the maximum volume of air which can be expelled in the first 0 75–1 0 second during an estimation of the vital capacity

There is disagreement on whether the resting ventilation is increased or not, but there is a preponderance of evidence in favour of an increase of respiratory rate at rest in the later stages of the disease Many observers have stressed the usefulness of exercise tests to uncover deficiencies not apparent at rest In Europe the exercise has usually been on a bicycle ergometer, and the work level increased by stages until the subject could do no more The indices of impairment are then the maximum load achieved and the ventilation or oxygen consumption for this or a lesser load For a given load the ventilation is usually found to be increased above normal in the second stage and sometimes in the first, but in the third stage the low exercise capacity usually limits the test In America, a stepping test has often been used with submaximal loads, and has not been standardized for weight so that the work done depends partly on the build of the subject The exercise ventilation (but not always at a 'steady state') is expressed as a ratio of the maximum breathing capacity to give an index of dyspnoea However, an index of this type has not been related to the stage of pneumoconiosis in any large group of subjects

There is universal agreement that arterial oxygen saturation at rest is not altered in the first two stages but is reduced below 90 per cent in the third Polycythaemia is rare On exercise there is a lowering of oxygen saturation in some cases and a rise in others The change has not been closely studied in relation to radiological appearances In German reports it is usually assumed that the limit of exercise tolerance is set by the oxygen debt,

* International Classification (1930)

Other papers were [illegible]
function for comp [illegible]
with measurement [illegible]
exercise assessment, and David (1950) estimated the oxygen saturation of arterialized ear capillary blood by the Roughton Scholander micro-method Pelnar (1950) described his method (p 18) for the simultaneous estimation of ventilation equivalents for oxygen and carbon dioxide, and concluded the best measure of pulmonary function by this method was obtained by adding the sum of the resting and maximum equivalents, equivalents during the recovery period were very variable

In Russia, vital capacity measurements on a group of 431 cases of silicosis and on 96 normal control cases were made by Evgenova (1948) The average vital capacity decreased with increasing silicosis though those in the first stage had a higher average capacity than the normal men The authors attributed this increase to the early development of compensatory emphysema in the first stage, though the difference of the means was clearly not significant Exercise tests were also used but only respiratory rate and pulse rate were recorded

In Italy, Caccuri and Di Lauro (1949) examined a small group of 12 cases of [illegible]

subjects were examined [illegible]

than the fibrosis, though he does not state how the emphysema was measured

Conclusions

One of the most striking features of previous work comparing lung function with radiological appearance is the lack of balance between the care with which the physiological measurements were made and the lack of precision in describing the radiographs In the majority of papers the radiographs were divided into three groups, and in the last group all cases with massive shadows were included irrespective of size It is probably no accident that McCann *et al* (1934), who divided their radiographs into six groups, have reported a closer relationship between function and the radiograph than the majority of workers, and that Motley *et al* (1949) found no relationship when studying a group in which two thirds of the cases were in the last group Ruyssen (1951) and Guillet (1951) on the other hand used the classification of Eck and Hanaut but found that the number of possible groups was too large to allow satisfactory analysis It seems reasonable to conclude that one cause of the failure to relate function [illegible]

The tests of function have varied from the simple exercise test used by Hart and Aslett (1942) to the complex indirect methods of measuring ventilation perfusion ratios used by Rossier, Bucher and Wiesinger (1947) and Motley, Gordon, Lang and Theodos (1950) As Lang (1947) noted, increasing the complexity of the tests has not in general improved the relationship between the

carry out and has a small random error, it must be presumed that there is a considerable difference dependent on the constitution of the groups Hart and Aslett (1942) and Wright (1942) used a group of working miners as their controls. Kadlec and Vyskocil (1950) chose a group of men who had never worked in dusty conditions, and they found a big difference in the maximum breathing capacity

literature as normal which have often been derived by different methods and in populations from other countries Examples and theoretical limitations of such pr

(1

advanced stages of disease tend to occur in the older subjects. Satisfactory separation of the possible effects of age and disease has not been achieved in

workers have grouped all their cases together irrespective of the process causing the disease Exceptions are Hart and Aslett (1942) and Motley, Gordon *et al* (1950), who examined only coalworkers, and Craw (1947), who examined only

common in silicosis, leads to a small lung volume without compensatory emphysema and to a greater disability for a given radiological disease stage

It is of primary importance to establish firmly the relation of function to

there is reason-

be prevented by

time when the

earliest changes have already appeared in the radiograph but have not yet reached the nodular stage, and when the subject still has no disability (Cochrane, Fletcher, Gilson and Hugh-Jones, 1951) A practical scheme of preventive medicine based on this use of the radiograph can only be justified if there is a reasonably good relationship between pulmonary function and radiological disease stage For if at the age of 50 the miner with massive shadows is not appreciably more disabled than the man with the earliest radiological changes specific of pneumoconiosis, the use of periodic X ray examinations would be of no avail in eliminating the disability

The review of the l

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errors are

report is an account of an experiment designed to relate lung function to age and disease in coalminers

although this has never been proved The other viewpoint is that when the ventilation reaches a high proportion of the maximum breathing capacity (approximately 70 per cent) the limit is set by the severity of dyspnoea whether or not severe desaturation of the arterial blood has occurred

Impairment of the intrapulmonary gas mixing has not been extensively studied in relation to the radiological appearance

It is generally agreed that cor pulmonale is not produced by the early stages of the disease When it occurs later it is often difficult to detect by clinical or even electrocardiographic examination It is thought to be related more closely to the residual air percentage of total lung volume than to the extent of the [illegible]

or more tests were measuring so nearly the same function that the number of tests could be reduced without appreciably detracting from the usefulness of the information gained Only a few tests had been related to the clinical assessment of disability for example the maximum breathing capacity dyspnoeic index and the residual air percentage of total lung volume but others for example the impairment of intrapulmonary mixing had been considered of major functional importance without establishing their relation to the best overall test of dysfunction—the man s complaint of breathlessness

Pneumoconiosis can only be diagnosed from the radiograph and the industrial history All agree that in the early stages many individuals have no symptoms Thus the population of subjects with pneumoconiosis can only be defined by radiological surveys in the area under investigation Statements of the relation of pulmonary function to the radiological appearance are therefore only [illegible]

There is another way in which the study of such groups will distort the impressions of the interrelation of radiograph and function Function tests cannot be made on all the patients who apply for treatment or assessment and it is those with a striking discrepancy between disability and radiograph who are most likely to be fully investigated This applies both to men with slight evidence of pneumoconiosis and severe disability and also possibly those with little disability but advanced radiographs This factor may have influenced the results of some of the observations by the French German and Swiss groups but probably not those of Motley and others who were careful to study all available cases even though their selection was already biased towards those with disability by their use of a hospital population

The assessment of the effect of silicosis or pneumoconiosis on lung function implies a definition of normal with which to make the comparison This is far [illegible]

different observers on large groups of normal subjects As the test is easy to

TABLE 2

Plan of the experiment showing the number of subjects in different groups studied

Age group	No of subjects in the following categories					
	Normal non miners N	Normal miners NM	Miners with pneumoconiosis			
			Simple 1/2	Simple 3	Complicated B	Complicated D
25	10	—	—	—	—	—
35	10	8	8	8	8	6*
45	10	8	8	8	8	8
55	10	8	8	8	8	8

* Only 6 subjects could be found with very advanced disease in this age group

The normal control group was increased to include 10 subjects instead of 8 at each age in order to establish the relation between age and test results in normal subjects more precisely an extra group aged 25 was also added A group of working miners who had less radiographic abnormality than category 1 simple pneumoconiosis was also studied, since preliminary analysis of the results showed evidence of an unexpected difference between the men in the earliest stage of simple pneumoconiosis and the normal control subjects

will be used

Group 1/2 refers to a group consisting of approximately equal numbers of men belonging to groups 1 and 2

Group 3_{45} refers to the group of 8 men with simple pneumoconiosis, category 3 of average age 45

Group 3 refers to all 24 subjects in this radiological category

The examinations and tests which are explained in detail in the section on Methods (p 34) were as follows

Clinical
Cardiological
Chest X ray
Standard exercise test
Blood oxygen saturation
Maximum voluntary ventilation
Vital capacity
Adrenaline test
Total lung capacity (closed circuit spirometry)
Gas mixing and transfer (open-circuit spirometry)
Movement of diaphragm
Anthropometry

Men were selected in advance according to the criteria given below and then asked to attend for clinical examination functional tests and radiography all

PART II. THE MAIN INVESTIGATION

1. PLAN OF THE EXPERIMENT

A OBJECTIVE

THE main experiment was planned with a double objective, to determine

(1) the nature of the disturbance of lung function in miners with pneumoconiosis and its relation to age and the radiological severity of the disease,

(2) the interrelation of a group of lung-function tests in order to find what functions each test measured and the extent to which one overlapped with another, and thus to determine the most suitable combination of tests for various purposes, especially for the assessment of disability in men with pneumoconiosis

The experiment was not intended to discover the extent of disability caused by pneumoconiosis among miners in South Wales Since pneumoconiosis can only be diagnosed by the radiograph, such an object would have required an exact knowledge of the radiological severity and age distribution of all miners and ex miners in South Wales and the sampling from a defined population This information was not available and in any case the population was then a changing one* (Hugh-Jones and Fletcher, 1951)

Our first objective made it necessary for us to apply several tests to a large number of subjects, thus we had to choose tests of high discrimination which were simple in execution for both subject and observer, since the complete schedule of tests had to be satisfactorily completed on 4 to 6 outpatients each day In these circumstances we learnt more about the practical limitation of [illegible]

our studies of intrapulmonary gas mixing and blood gas-transfer, we developed a new technique of combined helium and carbon monoxide inhalation which was rapid in execution and required no blood sampling or blood gas analysis This gave results which we find of sufficient interest to warrant full analysis beyond that required for our first objective The rest of this report is therefore divided into three parts The first (Part II) describes the relation we observed between lung function and age and the radiological stages of pneumoconiosis, the second (Part III) comprises the further theoretical analysis of our results to show how they contribute to a better understanding of the fundamental properties of the lungs, while the third (Part IV) is an attempt to interrelate the different tests of lung function in pneumoconiosis

B DESIGN

The experiment was planned on a balanced (orthogonal) design in relation to age and radiographic appearance It was decided to apply the tests to subjects representing four radiological stages of the disease, in three age-groups, together with a control group of non-miners with normal chest radiographs

The final plan of the experiment is shown in Table 2

* Recent radiological surveys (Cochrane, Cox and Jarman, 1952) of the entire population of one South Wales mining valley permit tentative interpretation of the results of this experiment as typical of a mining community in South Wales (see p 131)

syphilitic carditis In practice very few men were rejected on this account (see Table 4, p 32)

There was no attempt to make the normal groups a collection of supernormals, the criterion of normal being the average man in the street who had no detectable abnormality by the usual clinical methods The exclusion of men with a history of bronchitis among the miners would have been theoretically unjustifiable since this condition may result from pneumoconiosis

Source of Subjects

Normal Subjects

(*a*) The officers in charge of two local Ministry of Labour and National Service Employment Exchanges were asked to send along any men who were within the age limits chosen for the investigation, and who had not been miners or were not physically handicapped to an extent which would prevent them performing an exercise test Those who were willing to come were paid the standard rate (30s a day) for a single day's employment We obtained 28 men from this source, one ultimately being surplus

(*b*) Thirteen subjects were obtained from the technical staff of Llandough Hospital and the Pneumoconiosis Research Unit These were mostly in groups N_{25} and N_{35}

Miners

Over 1000 X ray films were examined in the course of selection, so as to choose good radiological examples of the required stages of pneumoconiosis These films represented men who had been radiographed (1) by the P R U as inpatients or outpatients during survey work in the previous three years, (2) by the Welsh National Memorial Association in the course of surveys in various parts of the coalfield (3) by the Pneumoconiosis Panels at both Cardiff and Swansea

Most of the miners showing no radiological evidence of pneumoconiosis came from the 250 face workers of one bituminous mine Fifty four of those in the appropriate age groups who volunteered were asked to attend for preliminary radiological and clinical examination, of these, 35 were of a suitable age, X ray and industrial history and were tested in the main experiment, the majority being suitable for the NM group and the remainder for other radiological groups where needed

Lapses and Rejects

These fall into two groups men who were asked to attend but did not do so (28 lapses) and men who were examined and tested but not included in the final analysis (27 rejects) The reasons for these lapses and rejections are given in Tables 3 and 4 on p 32

Only in category D is there a special reason for lapsing, here, of the 30 miners first selected, 4 did not attend because of illness or death This category, therefore, is probably biased towards the fitter men Of the rejects, the majority were simply surplus to the plan, those omitted were the men attending after the groups were filled In only 4 out of a total of 185 subjects tested were there sufficient technical faults to reject the case and select another The standard of co-operation on the part of the subjects was very high, which showed that it was feasible to apply relatively complex tests to a group of untrained subjects

of which were done on any one subject within one day, 4 to 6 men were seen daily between May and July, 1949 The daily time table was so arranged as to minimize the possible effects of one test on another Each day men were tested and examined in an arbitrary order until the complement in each age/X ray group had been filled There were finally a few surplus subjects (see Table 4, p 32) because extra men had to be asked to attend in case of lapses as the investigation proceeded The extra men were not included in the analysis because of the increased complexity of statistical treatment in groups of different numbers

C SELECTION OF SUBJECTS

Criteria for Selection

Age

To obtain as sharp a differentiation as possible with respect to age, an attempt was made to restrict the subjects to an age of $\pm$ 3 years about the nominal age of each group This was not always possible in the groups where there was a shortage of men from whom to choose. Ages were recorded to the nearest year at the time of the experiment

Chest Radiograph

[illegible]

of four observers in consultation in accordance with the proposals subsequently published by Fletcher and Oldham (1949, 1951)

Industrial History

In the groups of miners, at least 10 years' exposure underground to coal or mixed coal and stone dust on the coal face was required

In the normal group an attempt was made to choose subjects with no previous mining experience or exposure to any dust hazard, this was not quite achieved since so many men attending the Labour Exchanges in South Wales have at some time done a little mining

Criteria for Rejection

Men were only rejected for one of two reasons, as follows

Injury

Men were excluded if they had any injury to the legs or the chest which might have prevented them carrying out the exercise test or produced sufficient damage to affect their lung function (e g an old haemothorax)

Other Diseases

Men with diseases likely to affect the cardiopulmonary function were excluded, in particular those with chest diseases other than pneumoconiosis, severe anaemia, hypertension (B P >160/100), cardiac diseases clearly not due to pneumoconiosis, e g left heart failure, auricular fibrillation, rheumatic or

syphilitic carditis. In practice very few men were rejected on this account (see Table 4 p 32)

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TABLE 3

Men who were selected for the main experiment but were not tested

Group	Reason for lapse			Total
	Refused	Ill or dead	No reply	
N	(4)*	—	—	(4)
NM	(2)	—	—	(2)
1/2	1	—	3	4
3	3	1	4	8
B	4	—	2	6
D	—	4	—	4
Total	(14)	5	9	(28)

* Figures in parenthesis may not be quite exact

TABLE 4

Men who were examined and tested in the main experiment but rejected from the final analysis

Group	Reason for rejection				Total
	Surplus	Hypertension	Other diseases	*Technical* failure of tests	
N	1	4	—	3	8
NM	1	1	2	—	4
1/2	3	—	—	—	3
3	4	—	1	—	5
B	2	—	1	—	3
D	2	1	—	1	4
Total	13	6	4	4	27

Evaluation of the Sample

The final sample of men tested and included in the analysis well fulfilled the aim of the experimental plan

Age

In the majority of groups the actual mean age did not deviate more than 0 5 years from the nominal age of the group The largest deviation was 1 3 years in group N_{45} The range of ages within the groups was larger in the group of advanced pneumoconiosis

Radiological Category

... of the individual subjects given in Table I, approximated very closely to the ideal laid unction and radiographic appearance were

closely related, group 1/2 might appear slightly more functionally impaired than they should on account of the high proportion of category 2 cases which

mediastinum

Height and Weight

The individual stem heights, heights and weights given in Table I show that the sample was satisfactory in that there were no individuals at the extremes of height or weight, nor was any one group seriously unbalanced for either variable

Certification for Pneumoconiosis

In general, men in groups NM and 1/2 were uncertified, and in groups 3, B and D were certified (Table II, p 230) Certification refers to the Workmen's Compensation Act (1925); it depended partly on a clinical assessment of disability by the Medical Board of the Ministry of National Insurance The new National Insurance (Industrial Injuries) Act (1946) only came into operation at about the time of the experiment and did not affect the sample

Mining Experience

mixed dusts on the coal-face The group mean exposures increase with age, as would be expected The miners without evidence of pneumoconiosis have if

the mine prematurely on account of the disease

Subdivision of the exposure into the years worked in the three principal kinds of coal (anthracite, bituminous and steam) showed that the groups were not homogeneous in this respect We cannot determine from our observations whether the type of coal affects the degree of disability for comparable radiographic appearances, but separation of men according to the years they worked in stone as opposed to coal did not reveal any striking differences between the groups The average exposure to stone-dust was approximately one tenth of that to coal-dust

Employment

With the exception of group D_{65}, the majority of men were in some form of

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II. METHODS

1. Terminology, Abbreviations and Symbols

A DEFINITIONS

A group of physiologists in America (Pappenheimer and others, 1950) have suggested a standard set of definitions for the lung volumes and some symbols for the principal variables commonly measured in respiratory physiology, both in the gas and blood phases This was a logical development from the proposals made by Christie in 1932, and was a notable advance, since the proposals were backed by many eminent American physiologists who agreed to use them in their future publications

In this report we shall generally use from now on the American terminology, except that we have extended it where necessary to cover a wider physiological field In choosing terms we have kept two principles in mind

1 Where possible only one word is applied to a group of measurements recorded in the same units, unless another term is so firmly established as to make a change difficult or impossible

2 Where there is a choice between words, the same words as are already in current use in engineering, physics or chemistry are kept if they are physiologically applicable, and, where possible, words with different initials for different measurements are used since this avoids confusion in abbreviations

Of course, no terminology covers the very important qualifying statements required when expressing results, for example, the posture of the subjects, their sex, the use of the mean or maximum of a set of figures, the temperature correction used, etc We define these variables in the appropriate sections which describe the methods

The terms and their abbreviations which we shall use in this report and which may require explanation are given in Table 5

Capacities and Volumes of the Lung

These terms should be clear from Fig 1, which is essentially the same as that given by Pappenheimer *et al* (1950) except ... capacity and residual ... than ... vo ... ns, expiratory ... I ... ore convenient ... me ... ratory reserve ... e same unit offends our first principle stated above ... and 'volume' for measure- ... (Comroe, 1950) Volume is perhaps the more logical, since 'capacity' can be used to mean 'maximum ability' However, we have used 'capacity' as well as volume because 'vital capacity' is so firmly established The A ... authors have followed the example of Lindhard (1927) in using this ... functional su... of the lung, and we believe a convenien... between 'vo... 'capacity' can be made in resp... use the ... volum ...

the total amount ... is a term ... in excess of that ... the subject ... within certain lim... time ... the ... of oxygen' used ... work ... is ... (1923)

TABLE 5

Physiological terms and their abbreviations

Terminology	Abbreviation	Equivalent terms in previous publications
	Capacities (litres)	
*Total lung capacity	T L C	Total lung volume (T L.V.)
*Inspiratory capacity	I C	Complementary air (C A.)
Expiratory capacity	E.C	Complemental air Supplementary air Reserve air (Rv.A.)
*Vital capacity	V C	
Residual capacity	Rd.C	Residual air (Rd.A.) Residual volume (Rd V.)
*Functional residual capacity	F R C.	Functional residual air (F R.A.) †(Mid-capacity) Normal capacity
	Volumes (litres)	
*Tidal volume	T V	Tidal air (T.A.) Breathing air
*Inspiratory reserve volume	I R V	Complementary air minus tidal air Complemental air
*Expiratory reserve volume	E R V	Complemental air minus tidal air Supplemental air Reserve air
Exercise excess volume	E E V	New term (see text)
	Ventilation (litres/unit time)	
Resting ventilation	R V	Resting minute volume
Exercise ventilation steady state	E.V s	Exercise minute volume (at a steady state)
Maximum voluntary ventilation	M V V	Maximum breathing capacity (M B C.) Maximum voluntary capacity (M V C.)
Maximum exercise ventilation	M E V	New terms (see text)
Standardized excess ventilation	S E.V	
Standardized ventilation	S V	
	Diaphragm movement (cm.)	
Total diaphragm movement	T D M	
Inspiratory diaphragm movement	I D M	Complementary diaphragm movement
Expiratory diaphragm movement	E.D M	Reserve diaphragm movement
Resting diaphragm level	R.D L.	
Tidal diaphragm movement	Td.D M	

* Terms used in the American nomenclature (Pappenheimer and others, 1950)

† Mid-capacity is the F R.A. together with half the tidal volume

Diaphragm Movement

The terms used for diaphragm movement have already been defined by Wade and Gilson (1951), they are only modified here to conform to new terms for the lung capacities

B SYMBOLS

In formulae and equations we have used the standard American set of symbols as far as practicable However, since in this report we are concerned with the gas-phase only and use no equations dealing with blood we have omitted the generic symbol for volume V in our equations, it being understood that all volumes refer to the gas-phase Thus, we have used T for tidal volume instead of V_T

Our symbols are shown in Table 6

TABLE 6

Symbols

	General
V	volume
$\dot{V}$	ventilation (volume/unit of time)
P	pressure
* C	concentration (gas phase)
M	mass of gas
f	frequency or rate (e g breaths/unit time)
t	time
D	diffusing capacity in general, here applied to the lung (vols/unit time/unit pressure difference) e g Dco = diffusing capacity of the whole lung
K	physical constant, here applied to the diffusion constant e g Kco = diffusion constant of the lung membrane for CO (vols /unit time/unit pressure difference/unit area/unit thickness)
B	barometric pressure
λ	partition coefficient
≏	approximately equal to
$\sum_{r=a}^{b}$	sum of the quantities with subscript r for all values of from a to b
$\bar{x}$	mean (average) of the variable quantity x
r	coefficient of (linear) correlation between two statistical variates x and y $r = \Sigma (x-\bar{x}) (y-\bar{y})/\sqrt{\{\Sigma (x-\bar{x})^2 \Sigma (y-\bar{y})^2\}}$
	Specific volumes (gas phase)
* F	functional residual capacity
T	tidal volume
d	dead space
Te	effective tidal volume (T–d)

* Symbols used with a different meaning from that attached to them in the American classification

Suffixes

a — arterial
E — expired gas
I — inspired gas
A — alveolar gas
s — steady state
m — machine (i e Cm — gas-concentration in machine as opposed to lung Vm = volume of closed circuit machine)

Subscripts

A B etc — subdivisions of gas volumes undergoing different rates of gas replacement e g F_A T_A etc proportions of F T etc. taking part in phases of replacement A B etc
90 99 etc — degree of gas replacement in percentage units
r s — r^{th} s^{th} breath after start of experiment (e g Cm_r = concentration of gas in the machine at the r^{th} breath)

Special symbols for gas replacement experiments (uptake)

* q — expansion ratio† of lung as measured on open-circuit apparatus = F/(F+T)
* q_A — expansion ratio of lung as measured on open-circuit apparatus in phase A — $F_A/(F_A+T_A)$
* q — expansion ratio of lung as measured on open-circuit apparatus for corresponding Te — F/(F+Te)
* Q — expansion ratio measured on closed-circuit apparatus = $\frac{F}{F+T} \cdot \frac{Vm-T}{Vm}$
* Q — expansion ratio measured on closed-circuit apparatus for corresponding effective tidal volume (Te) = $\frac{F}{F+Te} \cdot \frac{Vm-Te}{Vm}$

(*a*) *Increment curves*

N^{Th} — [illegible] ber
N — [illegible] of breaths for 90% gas replacement
y_r — rejection ordinate at r^{th} breath (i e C_{E_0} C_{E_1} C_{E_r})
$1-y_r$ — acceptance ordinate at r^{th} breath

(*b*) *Accumulation curves*

N^{Th} — theoretical number of breaths
N — observed number of breaths
z_r — rejection ordinates $\left(\text{i e } C_{E_r} = \sum_{r=0}^{r} C_{E_r} \Big/ \sum_{r=0}^{\infty} C_{E_r}\right)$
$1-z_r$ — acceptance ordinates

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* Symbols used with a different meaning from that attached to them in the American classification

† Other authors (e g Birath, Bateman) have used the term dilution ratio

Diaphragm Movement

The terms used for diaphragm movement have already been defined by Wade and Gilson (1951), they are only modified here to conform to new terms for the lung capacities

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* C	concentration (gas phase)
M	mass of gas
f	frequency or rate (e g breaths/unit time)
t	time
D	diffusing capacity in general, here applied to the lung (vols / unit time/unit pressure difference) e g D_{CO} = diffusing capacity of the whole lung
K	physical constant, here applied to the diffusion constant e g K_{CO} = diffusion constant of the lung membrane for CO (vols /unit time/unit pressure difference/unit area/unit thickness)
B	barometric pressure
λ	partition coefficient
$\simeq$	approximately equal to
$\sum_{r=a}^{b}$	sum of the quantities with subscript r for all values of r from a to b
$\bar{x}$	mean (average) of the variable quantity x
r	coefficient of (linear) correlation between two statistical variates x and y $r = \Sigma (x-\bar{x}) (y-\bar{y})/\sqrt{\{\Sigma (x-\bar{x})^2 \Sigma (y-\bar{y})^2\}}$
	Specific volumes (gas-phase)
* F	functional residual capacity
T	tidal volume
d	dead-space
Te	effective tidal volume (T–d)

* Symbols used with a different meaning from that attached to them in the American classification

Suffixes

a .. arterial
E . expired gas
I .. inspired gas
A . alveolar gas
s . steady state
m .. machine (i e Cm = gas-concentration in machine as opposed to lung Vm = volume of closed-circuit machine)

Subscripts

A, B etc subdivisions of gas-volumes undergoing different rates of gas-replacement, e g F_A, T_A etc, proportions of F, T etc. taking part in phases of replacement A, B etc
90, 99 etc degree of gas replacement in percentage units
r, s r^{th}, s^{th} breath after start of experiment (e g Cm_r = concentration of gas in the machine at the r^{th} breath)

Special symbols for gas-replacement experiments (uptake)

* q expansion ratio† of lung as measured on open-circuit apparatus = F/(F+T)
* q_A expansion ratio of lung as measured on open-circuit apparatus in phase A = $F_A/(F_A+T_A)$
* q′ expansion ratio of lung as measured on open-circuit apparatus for corresponding Te = F/(F+Te)
* Q expansion ratio measured on closed-circuit apparatus = $\frac{F}{F+T} \cdot \frac{Vm-T}{Vm}$
* Q′ expansion ratio measured on closed-circuit apparatus for corresponding effective tidal volume (Te) = $\frac{F}{F+Te} \cdot \frac{Vm-Te}{Vm}$

(*a*) *Increment curves*

N^{Th} [illegible] ber
N [illegible] of breaths for 90% gas-replacement
y_r rejection ordinate at r^{th} breath (i e C_{E_0}, C_{E_1}, C_{E_r})
$1-y_r$ acceptance ordinate at r^{th} breath

(*b*) *Accumulation curves*

N^{Th} theoretical number of breaths
N observed number of breaths
z_r rejection ordinates $\left(\text{i e } C_{E_r} = \sum_{r=0}^{s} C_{E_r} \Big/ \sum_{r=0}^{\infty} C_{E_r}\right)$
$1-z_r$ acceptance ordinates

---

* Symbols used with a different meaning from that attached to them in the American classification

† Other authors (e g Birath, Bateman) have used the term 'dilution ratio'

Statistical

The statistical significance of results is indicated by the value, or by upper and [illegible]

[illegible]

confidence that the effect being tested is present, e g

	$(P \simeq 0\ 01)$		$(P \simeq 0\ 40)$
Results significant	$(0\ 05 > P > 0\ 02)$	Results not significant	$(0\ 3 < P < 0\ 5)$
	$(P < 0\ 05)$		$(P > 0\ 05)$

C SPECIAL ABBREVIATIONS

For ease of reading we have used terms such as 'extent of disease', 'disease stage' or just 'disease' to refer to the abnormality due to pneumoconiosis on the radiograph This overcomes the use of the more cumbersome but correct 'radiological disease stage

2. Criteria for Choice of Tests

We have derived four criteria of 'usefulness' for the tests we used

(i) Simplicity
(ii) Repeatability
(iii) Discrimination
(iv) Validity

The first three criteria are used in assessing the value of each method as it is described Validity, which depends on the analysis of the results, is demonstrated in Part IV (p 202)

Simplicity

[illegible]

until rapid physical gas analysers improved their simplicity For example, carbon monoxide uptake was not a 'simple' test until the development of the infra red gas analyser

Repeatability

The closeness with which repeat readings agree on the same subject in the same physiological state is an approximate measure of the random errors of a method and is sometimes called 'accuracy' (see below) These errors include those arising in the apparatus as well as those produced by the variability of observers and subjects over a short time (usually within a day*) An analysis of the relative importance of these factors is required when attempting to improve the repeatability of a test

The repeatability may be determined from the scatter of a number of replicate measurements on one subject In functional tests this is usually impracticable because the many repetitions alter the physiological state of the subject An alternative, which we usually employed in subsidiary experiments separate from the main experiment, is to make duplicate measurements on a large number of

* The assumption is made that the day to-day variation in different groups is the same, his may not be strictly true

different subjects in order to obtain an estimate of the standard error of a single observation A similar estimate can be obtained from the residual error term of an analysis of variance on the results of experiments which provide repeat measurements on a number of subjects The use of the standard error of a single observation is not strictly correct, since in nearly all tests the error is not constant but increases proportionally with the magnitude of the reading

Discrimination

Two properties of a test are concerned in its discriminatory efficiency First, there is the difference between the mean values found in normal subjects and those found in subjects with advanced disease Secondly, there is the scatter of values found within the groups of normal and diseased subjects We express the

[illegible]

discrimination in the measurement of pulmonary function by a given test may be illustrated by an analogy with the measurement of length by a ruler to measure a long distance a ruler with coarse gradation may suffice, but to obtain the same precision in a short length, finer gradations are necessary Thus, the 'coarseness' of gradation (analogous to the scatter of function test results in any group of subjects) is important only in relation to the length to be measured (analogous to the range of test results between normals and abnormals) This criterion of discrimination is applicable to any functional test

An illustration of tests which have 'bad' and 'good' discrimination in pneumoconiosis is shown in Fig 3 where chest expansion is compared with maximum voluntary ventilation

A statistical measure of the discrimination ratio is the use of Student's 't' In this report we have used a corresponding measure which allows for the effects of age It was obtained from an analysis of variance of the results of the normal group (excluding N_{11}) and those for the group of the most advanced pneumoconiosis (group D) and is

$$\sqrt{\left(\frac{\text{variance between radiological groups}}{\text{error variance}}\right)^{*}}$$

It is emphasized that the discrimination measured by this ratio (D R) applies only to pneumoconiosis A similar index will be derived for 'emphysema' (p 140)

Validity

This is an expression of the extent to which the test measures what it is intended

[illegible]

* No significant interaction between age and X ray was found in any test

statistical analysis is necessary to separate all these components and to define how specific or valid the test is as a measure of any particular aspect of lung function

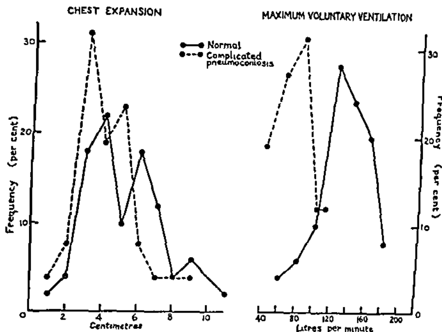


Fig 3 *Comparison of chest expansion and maximum voluntary ventilation as an example of the meaning of discrimination*

In chest expansion (poor discrimination) the abnormal subjects overlap with the normal almost completely in the maximum voluntary ventilation test the two groups are well separated 76 subjects (50 normal 26 complicated pneumoconiosis ages 33–58)

3. Clinical Methods

A full clinical examination was made for three purposes first, to compare clinical findings with the results of the physiological tests, secondly, to get some idea of the frequency of selected signs and symptoms for comparison with reports of other observers, and lastly, to ensure correct selection of subjects for age/X ray group (see plan of experiment, p 30) Subjects were examined by one clinician experienced in pneumoconiosis and frequently by a second independently Neither observer knew the results of any of the physiological tests nor the radiological groups of the subjects Full clinical histories and examinations were recorded on a pro forma but only the more interesting features were analysed

Certain clinical findings, which were to be compared with the physiological results, were expressed quantitatively on arbitrary scales as follows

Grading of Breathlessness

After a discussion with the subject, the observer had to answer the questions given below and so put the subject in one particular grade

	Grade	
Is the patient's breathing undoubtedly as good as other men of his own age and build, at work, on walking and on climbing hills and stairs?	0	Normal
Is the patient's breathing probably as good as other men of his own age and build at work, on walking and on climbing hills and stairs?	1	Normal
Is the patient able to walk with normal men of his own age and build on the level but unable to keep up on hills or stairs?	2	
Is the patient unable to keep up with normal men on the level but able to walk about a mile or more at his own speed?	3	
Is the patient unable to walk more than about 50–70 yards on the level without a stop?	4	
Is the patient obviously breathless on talking or undressing, or unable to leave his home because of breathlessness?	5	

Grades 0 and 1 were both conceived to be within the range of normal, grade 0 being added to see if those subjects deemed to be 'undoubtedly normal' with respect to breathlessness on exertion were different physiologically from the subjects in grade 1 In using the results, the grades were treated as if they formed a linear scale of units unless stated otherwise

In the grades in which categorization was more difficult (0–3), the comparative element with a 'normal' man of corresponding age and build was introduced It was hoped that this might slightly increase the precision (repeatability) of grading The gregarious social activities of miners in a hilly area like South Wales probably made this assessment easier than it would have been elsewhere The subject would often remember when walking with other men if he had to 'take a spell' (i e rest) on a hill

Bronchial Spasm

A system of marking based on the history and examination of each subject was used to obtain estimates of the average degree of bronchial spasm* for each group The detailed comments on the history section of the pro-forma were simplified to two grades tightness in the chest 'with colds only' or 'on other occasions as well' From the physical examination a wheeze on auscultation both over the trachea and the chest was recorded as 'absent', 'present' or 'marked' An audible wheeze over the trachea was occasionally present when no wheeze was heard over the chest, but for analysis the two separate observations are grouped together

Physical Signs in the Chest

It was decided to select certain physical signs from the chest examination
Fixity of chest
Barrel deformity of chest
Impairment of cardiac dullness
Impairment of liver dullness
Hyperresonance of percussion
Epigastric pulsation
Impairment of breath sounds
Intercostal recession on inspiration

* The word 'spasm' is used to mean a presumed constriction and does not necessarily imply obstruction caused by muscular contraction (see p 53)

5. Physiological Methods

In all tests the subject was sitting at rest unless otherwise stated, but not under basal conditions Gas-volumes were recorded at room temperature, saturated with water vapour The readings were then corrected and expressed as their equivalent volume at body-temperature, ambient pressure, and a water-vapour pressure of 45 mm Hg, the latter represents the degree of saturation believed to exist in the lungs The different spirometers used agreed within ± 1 per cent

A STANDARD EXERCISE TOLERANCE TEST

Full details of this test have been published elsewhere (Hugh-Jones, 1952) It was a clinical step-test modified so that each patient did a known and standard amount of exercise (350 kg m per minute for 5 minutes) Standardized exercise was chosen rather than an amount which varied with the weight of the patient because we wished to find whether the ventilation for a given amount of exercise was increased in pneumoconiosis

Both the step-height and rate of stepping were adjusted so that neither had ... between ... ological ... has been shown to be valid experimentally (Hugh Jones, 1952) The extra ventilation above the resting level caused by the standard amount of exercise was found by measuring the total volume of air exhaled per minute for an appropriate time before, during and after the exercise

Apparatus

Three pieces of equipment were used for the test (Plate 10) (1) a rigid platform, 9 in (23 cm) high, the height of which could be altered in ½ in increments by placing the appropriate number of boards on it; (2) a metronome for controlling the rate of stepping, (3) a low resistance gas-meter for measuring the ... the latter being

read to the nearest litre The resistance to expiration was about ... at a ventilation of 30 litres per minute

Procedure

The patient was weighed and the appropriate step-height and stepping rate for the standard amount of exercise were read from a nomogram (Fig 4) ... per minute is required, a ruler is placed

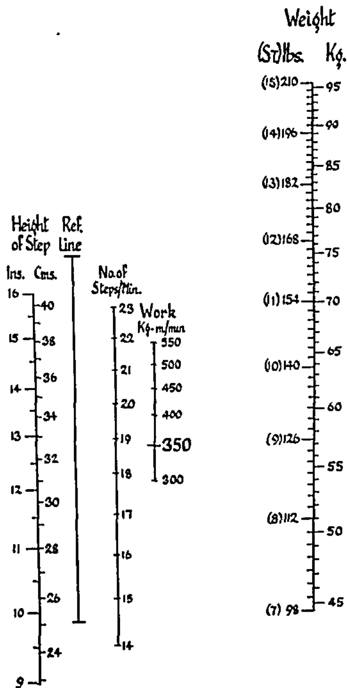


FIG 4. Nomogram used to standardize the work in the exercise test For method, see

and that measured directly by the Hellige colorimetric method was fairly satisfactory

TABLE 7

Comparison of oxygen saturation of blood from brachial artery and 'arterialized' ear lobe blood

Subject	Direct from brachial artery (Van Slyke analysis)			'Arterial from ear lobe (Scholander Roughton analysis)		
	O_2 content (Vol %)	O_2 capacity (Vol %)	Saturation (%)	O_2 content (Vol %)	O_2 capacity (Vol %)	Saturation (%)
1*	15 0	19 4	77	15 0	19 1	79
2	*21 1*	*22 3*	*95*	20 0	21 3	94
3	13 6	16 9	80	12 8	15 7	82
4	16 2	19 0	85	16 3	19 0	85
5	18 2	19 3	95	16 7	18 5	91
6	*15 0*	*16 7*	*90*	*12 7*	*14 7*	*86*
	Mean		87 0	Mean		86 2

* This arterial sample was analysed by the Scholander Roughton micro method

C VITAL CAPACITY

The vital capacity was measured on two separate occasions on each subject on different pieces of apparatus

Apparatus

(1) The vital capacity (V C) was recorded on the simple spirometer (Plate 11), also used for measuring the maximum voluntary ventilation This measurement of vital capacity is referred to as V C (Open) The principal dimensions of the spirometer were bell capacity 8 litres diameter 16 cm , weight 412 g , diameter of breathing tube 4 2 cm There was no carbon dioxide absorber or central core in the water chamber

(2) The vital capacity was also recorded on the closed circuit spirometer which was used for measuring the total lung capacity (Plate 12) This measurement is referred to as V C (Closed) The bell capacity of this apparatus was 8 litres, diameter 16 cm , diameter of breathing tube 2 2 cm The water chamber was fitted with a central core and there was a carbon dioxide absorber in the circuit

Procedure

For both methods the subject was seated in a comfortable upright posture ... nose clip For the measurement of V C (Open) he was instructed to ... and exhale

A trial run was followed by three tests ... effort Readings were only rejected if there was some obvious failure or difficulty in co-operation V C (Open) is the mean of at least two and usually three technically satisfactory records (see Gilson and Hugh Jones, 1949)

For the measurement of V C (Closed) the subject breathed through a rubber mouthpiece in and out of the closed-circuit apparatus (filled with oxygen) until the respiratory pattern became sufficiently stable to obtain a slope for the approximate measurement of oxygen uptake (3–4 minutes) The subject was instructed at the end of a normal expiration to exhale as deeply as possible and then to return to normal breathing Two or three estimations of expiratory capacity (E C.) were recorded at intervals of about 1 minute Next, two or three estimations of inspiratory capacity (I C) were made starting at the end of a normal expiration The V C (Closed) was computed by adding the expiratory and inspiratory capacities, each measured from the resting respiratory level drawn on the spirogram

Evaluation

The test ranks high for simplicity The open-circuit method needs less apparatus than the closed-circuit method but more co-operation by the subject We have found the standard error of a single observation to be approximately 50 ml for V C (Open) and 100 ml for V C (Closed) (Gilson and Hugh Jones, 1949) Rahn, Fenn and Otis (1949) and Whitfield, Waterhouse and Arnott (1950a) have reported similar standard errors Hugh Jones (1949) showed that there were considerable differences in the mean and scatter of normal values even when groups of several hundred subjects were compared Recent reviews giving normal values are those of Comroe (1950), Whitfield *et al* (1950a) and Needham, Rogan and McDonald (1954)

The simplicity of measurement has often led to the vital capacity being used as a test of lung function without an appreciation of its great limitations It is a measure of capacity without relation to time and is, therefore a poor test of function Christie (1932) pointed out that it requires for its measurement the practice of respiratory 'gymnastics' never used even in the severest exercise The wide variation even in normal subjects means that it is of limited use for measuring the deviation from normal Although its discriminating power is poor in emphysema (D R 3 17), it is relatively good in pneumoconiosis (D R 9 24) The measurement is essential for determining the subdivisions of the total lung capacity

D MAXIMUM VOLUNTARY VENTILATION

Apparatus

The spirometer described for measuring V C (Open) was used (Plate 11) The chain linking the bell to the counterweight passed over a wheel carrying studs which operated an electrical counter and added up the total number of contacts made, the space between each stud was equivalent to a volume of 270 ml Another set of contacts (controlled by a spring loaded capstan) closed when the wheel was revolving one way and opened when the wheel reversed, these operated a second counter which recorded the number of breaths The counters were in series with a switch, which was closed at the same moment that a stopwatch was started, and was released when the second hand of the watch reached 15 seconds Records of the pressure change at the mouthpiece using an electro-manometer with a high frequency response showed peak values of −7·0 cm water pressure on inspiration and +5·4 cm on expiration with a mean of approximately 1 5 cm in both phases when the maximum voluntary ventilation was 150 litres per minute Thus the resistance of the apparatus was low

Procedure

The subject, wearing a nose-clip sat in front of the apparatus and took the tube to the spirometer in both hands After a single deep inspiration, he inserted the mouthpiece and breathed out into the spirometer He was then instructed to breathe in and out as deeply and as fast as possible with the emphasis on depth When a smooth rhythm had been established the switch was closed and the watch started The noise and rate of movement of the volume recorder enabled the observer to encourage rate or depth of breathing as was necessary in order to maintain a maximum output

Calibration

Although the same apparatus is used, instrumental errors may be considerably greater in the maximum voluntary ventilation test than in the vital capacity [illegible]

of our apparatus and an account of an improved method for measuring maxi mum voluntary ventilation have been published (McKerrow in the press) We therefore give only a summary of the calibration here

The physical calibration of the apparatus was so complex that no simple correction factor was satisfactory Instead, a biological calibration against a Douglas bag method was used, over a wide range of values Fig 5 shows this calibration Twenty two male subjects, with a range of maximum voluntary [illegible] tested on a randomized [illegible] e there is almost perfect [illegible] id 120 litres per minute (Douglas bag estimate) the spirometer over reads with a maximum at one point by about 20 per cent Above 120 litres per minute there is no systematic error, the points scattering on either side of the line of perfect agreement [illegible] not due

[illegible] ag and the small range of maximum voluntary ventilation values where the error of the spirometer method may exceed 10 per cent it was decided not to apply a correction to all the results Where any conclusion might have been affected by this error, the results have been re examined critically after applying the correction McKerrow s detailed calibration of our spirometer leaves no doubt that our results in the main experiment are not in error, as a result of the apparatus we used, to an extent which affects the general conclusions we draw

Evaluation

The maximum voluntary ventilation is a simple test to perform The simplest apparatus required is two Douglas bags, a supply of carbon dioxide a low resistance valve a stop watch and a gas meter for measuring the volume of gas expired This equipment is cumbersome and slow to use if large numbers of subjects are to be examined A simple spirometer with an integrating device (Gray and Green 1945 Cournand, Richards and Darling, 1939, Gilson and Hugh Jones 1949) may introduce errors, although these may be reduced by

improvement of the apparatus (Bernstein, D Silva and Mendel, 1952, McKerrow, 1953) At present it seems necessary for each group of workers to establish their own normal values (Wright, 1950)

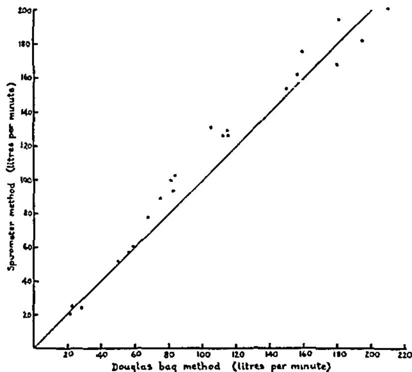


FIG 5 The relation between the maximum voluntary ventilation as recorded by the Douglas bag and spirometer methods on 22 male subjects The line is one of perfect agreement

The test requires rather more co operation on the part of the subject and skill by the observer than recording the vital capacity The standard error of a single observation was 7 5 litres in a group of normal and abnormal subjects (Gilson and Hugh-Jones, 1949) Despite the rather poor repeatability there is such a marked change in the maximum voluntary ventilation in pneumoconiosis that it shows the best power of discrimination of any single test (D R 12 69) Its discrimination in emphysema is also good (D R. 6 18) and much better than that of the vital capacity

The means, and scatter about the means, in our normal subjects are shown in relation to age in Table V, Appendix I (p 233)

E. ADRENALINE TEST FOR BRONCHIAL SPASM

We use the term 'bronchial spasm' physiologically to mean a state of the lung which can be altered abruptly by the administration of adrenaline Whether the alteration is due to a relaxation of the bronchioles, or to a shrinkage of the

mucosal surfaces, or partly due to a vasomotor change as suggested by Sheldon and Otis (1951), we did not attempt to determine

It is generally agreed that bronchial spasm can alter the results of some tests for example, vital capacity, maximum voluntary ventilation

Procedure

At the end of the day after completion of all other tests, the vital capacity and maximum voluntary ventilation were recorded The subject was then given 0 5 ml of adrenaline (1 1000) subcutaneously, and inhaled nebulized 'Riddobron'* from a Collison inhaler in a series of deep breaths over 2 minutes Vital capacity and maximum voluntary ventilation were immediately measured again

Administration of a fixed dosage in this manner does not necessarily produce a maximum effect in any particular subject (Rossier, 1949), but it is probably satisfactory for detecting the relative severity of spasm in different groups and for revealing individuals with marked spasm The dose was large enough to produce some subjective side-effects in about a quarter of the subjects

F CLOSED-CIRCUIT SPIROMETRY

A closed circuit spirometer filled with a mixture of 14 per cent heli oxygen was used for measuring the total lung capacity and the inequal ventilation The total lung capacity was calculated from the dilution c mixture in the spirometer after equilibrium had been reached The rate of cl of helium concentration between the start of the experiment and the estal ment of equilibrium reflected the rate of gas replacement in the lungs, and function of the tidal volume the functional residual capacity the natu the mixing processes within the lung the volume of the closed circuit appar and the response rate of the helium katharometer By correcting for the kn variables an estimate of mixing efficiency in the lung could be obtained

Apparatus

After passing through the carbon dioxide absorber, a p through a side circuit to the katharometer† at 2 litres per minute and back i the main circuit

An electromagnetic ink marker was used to record a series of points the k mograph corresponding to galvanometer readings as mixing between

is a record of the concentration of helium in the spiro from the start of the mixing process (curve A, Fig 7) By subtracting t

* A proprietary preparation similar to Nebula Adrenalin et Atropin Co (N F)

† Katharometer supplied by the Cambridge Scientific Instrument Company Grosvenor Street London Calsoda granules for absorption of carbon dioxide supplied by Kendra Ltd The Laboratories 5 Lodge Villas Woodford Green Essex

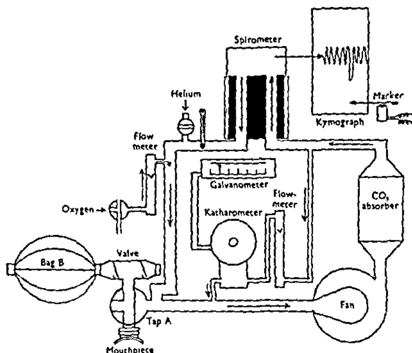


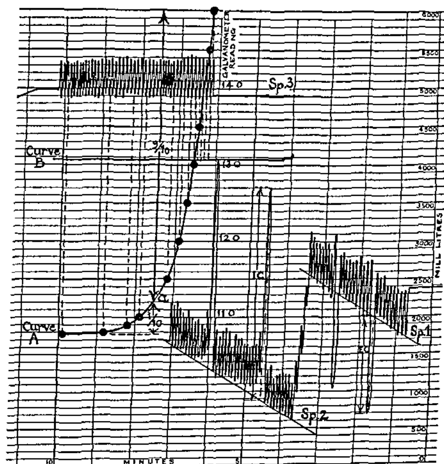
FIG 6 Diagram of closed-circuit spirometer The subject breathes from the oxygen-containing bag (B) while the spirometer is being adjusted On turning tap A the subject is brought into the spirometer circuit at a point of zero pressure (relative to atmosphere) and the supply from the bag (B) is cut off

concentration at any breath from that initially in the spirometer and expressing this difference as a fraction of the total fall in concentration between the start and end of the run, it was possible to plot a curve representing the accumulation of helium in the lungs breath by breath Such a curve will be called an 'accumulation curve, its relation to other curves representing the process of gas-mixing is discussed on pp 69 and 155 et seq

The derivation of an accumulation curve in the lungs is justified provided the mixing in the machine circuit is complete between every breath This was only approximately true, the curve obtained being influenced by the response time of the recording system (see Calibration below)

Procedure

First, a normal spirogram (Sp 1 and 2) was recorded (Fig 7) with the spirometer filled with oxygen, which gave an estimation of the rate of oxygen consumption and the expiratory and inspiratory capacities as already described At the end of this tracing, the subject was switched on to a supply of oxygen to complete the elimination of nitrogen from the lungs while the apparatus was being filled with helium and oxygen for the estimation of the functional residual capacity The katharometer is slightly sensitive to nitrogen so that this preliminary removal of nitrogen from the lungs is desirable for maximum accuracy.



back into the spirometer system After a few seconds' delay the galvanometer needle started to fall, first rapidly, then more slowly as the mixing process neared completion The experiment continued until the galvanometer did not fall as much as 0 03 per cent between observations at one minute intervals

During the period of equilibration the volume of the system was held constant by supplying oxygen at the rate indicated by the slope of the preliminary spirograms.

Presentation of Results

Total Lung Capacity

The principle of the method is that the total fall in the concentration of helium in the circuit is proportional to the volume added to the circuit when the subject is switched in Thus, the combined volume of the lungs and spirometer can be calculated from the final galvanometer reading according to the method of calibration of the instrument (see below) From this volume is subtracted the volume of the spirometer at the resting respiratory level of the subject and the remainder is the functional residual capacity The latter plus the inspiratory capacity is the total lung capacity

*Indices of Inequality of Ventilation ('Mixing Efficiency')**

The number of breaths required to achieve a given percentage of helium accumulation This has been used by some workers (p 188) as a simple index of mixing efficiency on the presumption that the greater the number of breaths required to achieve a given degree of gas replacement, the more unequal is the ventilation in different parts of the lungs It is not a satisfactory index, mainly because it is also dependent on the size of the tidal volume and functional residual capacity The number of breaths required for the accumulation of 50, 90 or 99 per cent of the final concentration of helium reached in the lung is used (symbolized here by N_{50}, N_{90} or N_{99}, respectively) These values can be obtained directly from the curve representing the galvanometer readings without plotting the actual accumulation curve in the lung For example, N_{90} is obtained by taking a point representing nine tenths of the total drop (a, Fig 7) From the interception of this line with the spirogram Sp 3 the number of breaths to which it corresponds is found

Overall index of inequality When a true measure of ventilatory inequality [illegible]
[illegible]
[illegible]
[illegible]
required were complete and equal mixing taking place throughout the lung at [illegible]
[illegible]
[illegible]
[illegible]
[illegible]

$$Cm_0 - Cm_r = Cm_0 \frac{F}{F + Vm}\left[1 - \left(\frac{F}{F + T} \quad \frac{Vm - T}{Vm}\right)^r\right] \qquad (1)$$

where r is the number of breaths, F is the functional residual capacity, Vm is the volume of the closed-circuit machine when the mixing process is started at the end of a normal expiration, and T the tidal volume But the total fall at complete mixing is

$$Cm_0 - Cm_\infty = Cm_0 \left(\frac{F}{F + Vm}\right) \qquad (1a)$$

* Throughout this report the term 'mixing efficiency' will generally be used as synonymous with degree of inequality of ventilation' The latter, though clumsy, is more exact

Dividing equation (1) by (1a), the fall in concentration up to any breath r as a fraction of the total fall is

$$\frac{Cm_0 - Cm_r}{Cm_0 - Cm_\infty} = 1 - \left(\frac{F}{F+T}\ \frac{Vm - T}{Vm}\right)^r \qquad (1b)$$

The ratio

$$\frac{F}{F+T}\ \frac{Vm - T}{Vm}$$

is called the 'expansion ratio' for the closed circuit *system to which we give the* symbol Q

The mixing efficiency of a subject may be expressed as the deviation of the observed curve from the theoretical one for perfect mixing, for the same tidal volume and functional residual capacity Bates and Christie (1950) expressed the deviation from perfect mixing by a 'mixing efficiency index' We shall refer to their index as the 'index of overall ventilatory inequality (I_O) to distinguish it from other similar indices derived from open-circuit data (p 69 et seq) which are based on deductions about the nature of different kinds of ventilatory inequality that may be found in the lung Thus in symbols

$$I_O = 100\ N_{90}^{Th}/N_{90} \qquad (2)$$

where N_{90}^{Th} is the number of breaths derived for the theoretical model and N_{90} is the observed number This index can be calculated without plotting either the theoretical or practical curves equation (1b) states that the concentration in the r^{th} expirate is a fraction $1-Q^r$ of the final concentration, if this fraction *is to be 0 9, $Q^r = 0\ 1$ and*

$$r = N_{90}^{Th} = \log_{10} 0\ 1/\log_{10} Q$$
$$= -1/\log_{10} Q$$

Hence

$$I_O = -100/N_{90} \log_{10} Q \qquad (3)$$

Now we found, like Bates and Christie, that in experiments with a model lung in the form of a pump, in which mixing was completed between each 'breath', an I_O of 100 per cent was not obtained mainly through delay in the response of the galvanometer but also though to a small extent, through incomplete mixing within the spirometer system between each breath They scaled their results up by 100/8[illegible]
factor was 100/85 [illegible]
for the initial lag [illegible]
simple proportionate scaling up may be justified over quite a wide range of respiratory rates though when the rate is very slow it is an over-correction compared *with normal rates, since the galvanometer then responds more* completely between each breath (see Calibration below)

Calibration

Galvanometer katharometer system In order to determine what added volume corresponds to a given fall in galvanometer reading it is necessary to take account of the dead space of the apparatus, the volume of the tubes fan, etc When the dead space is known a curve can readily be plotted relating galvanometer *reading and volume in the system*

The dead space is usually calculated by an external gas analysis method for example, by starting with the apparatus full of air and the bell at zero position, adding oxygen and then after thorough mixing removing a *sample* and analysing for the percentage of oxygen with the Haldane apparatus

the bell set at an arbitrary level nearly zero The volume was noted (V_0) Sufficient helium was added to the circuit to give a full-scale deflexion on the galvanometer (15 per cent helium) and the new volume of the bell noted (V_1) Oxygen was run into the spirometer to within about 1 litre of its full capacity and the volume again noted (V_2) More helium was slowly added to bring the galvanometer back to its original full scale deflexion The final volume (V_3) was recorded

First volume of helium added (H_1) $= V_1 - V_0$
Second volume of helium added (H_2) $= V_3 - V_2$

Now, if Vm is the dead space of the machine,

$$\frac{H_1}{Vm + V_1} = \frac{H_1 + H_2}{Vm + V_3}$$

or

$$Vm = \frac{H_1V_3 - (H_1 + H_2)\,V_1}{H_2}$$

In terms of the ratio of the helium volumes added, $R = H_1/H_2$,

$$Vm = RV_3 - (R+1)\,V_1$$

Using this method, readings agreed within a maximum deviation of 80 ml in a mean of 4755 ml The results were more consistent than the measurements

spirometer reading of 2000 ml Unit volumes of oxygen were again added until the bell was full In the first part of the curve the galvanometer reading was plotted against the spirometer volume The second part of the curve was corrected for the gas expelled by adding the volume of the machine to the spirometer reading, multiplying by $\frac{Vm+5000}{Vm+2000}$, and then subtracting Vm

The katharometer responds to the mass of helium and is therefore slightly affected by barometric and temperature variations It is also affected by the

multiplying by $G_{[illegible]}/G_{[illegible]}$

Interpretation of the mixing curve can only be made if something is known about the response rate of the recording system to changes in helium concentrations With the system filled with 14 per cent helium to the usual starting level for a mixing experiment (1500 ml), the addition of 200 ml of oxygen as rapidly

as possible caused an initial lag of 6 seconds before any response in the galvanometer occurred and a *final stable reading* was reached in about 20 seconds It is probable that the first part of the mixing curve is largely determined by the characteristics of the galvanometer-katharometer system During the latter part of the mixing process, when rate of change is slow, the effect of the instrumental lag on the shape of the curve is small

The output of the fan was sufficient to give one complete gas change every 4–5 seconds Increasing the fan speed by approximately 25 per cent did not affect the response rate of the system on suddenly introducing a known volume of helium The flow through the katharometer side circuit was fixed just below the level at which unstable readings occur (2 litres per minute)

[illegible] there are no

helium during one hour with the fan running and all the taps closed

Calibration of whole apparatus A piston-type pump with a variable stroke (i e tidal volume), rate and volume above the piston (i e functional residual capacity), in which a fan ensured complete gas mixing between each 'breath', was used as an 'artificial lung' for calibrating both the closed and open-circuit spirometers

Whereas the open circuit machine gave perfect agreement between the theoretical and practical mixing curve (see p 75), this was not true of the closed-circuit apparatus The lag of the katharometer galvanometer system distorts the curves (see Fig 8) and the overall 'mixing efficiency index' (I_0) was less than 100 per cent The initial S shaped part is caused by the galvanometer lag

The amount of lag depends on the rate of breathing so that the I_0 of the lung changes slightly at different breathing rates In Fig 9 the calibration of our machine for six different breathing rates is given and compared with three points quoted from Bates and Christie (1950) The machines appear to behave similarly, though our results show the expected relation to breathing rate more clearly

Evaluation

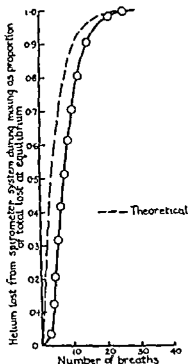
Lung capacity and its subdivisions The open and closed circuit methods of measuring the functional residual capacity have given concordant results, but we prefer the closed circuit method on grounds of simplicity and reduction of errors (Gilson and Hugh-Jones, 1949) More recently, the simplicity has been disputed by Fowler (1950), but we do not agree with *his criticism* *Open-circuit* [illegible] closed

[illegible] 955) A

[illegible] rometer

[illegible] ally no

maintenance is required, now that the [illegible] ing the katharometer itself, calibration is simple even in laboratories where there is no provision for the usual methods of gas analysis Estimations are quicker to make than on the open-circuit method and the apparatus is much more [illegible]



[illegible]

$N^{1.5}_{90} = 10·2$, ∴ $I_e = \frac{[illegible]}{12·3-1} = 90\%$ (one breath being subtracted from the denominator as a correction for lag as described in the text)

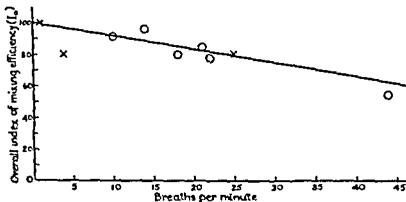


FIG. 9 Effect of breathing rate on the mixing efficiency index (I_e) of the 'artificial lung' estimated on the closed-circuit spirometer O = our results, X = results reported by Bates and Christie The straight line is the one of best fit (graphical) for our results.

manometric gas-analysis, defects may not be revealed until after the subject has left the laboratory

The *repeatability of closed-circuit estimates of the functional residual capacity* in normal subjects appears to be about the same as that for the open-circuit and is about 3 per cent of the average normal value The standard error of a single observation has been found to be about 100 ml by most workers (Gilson and Hugh-Jones, 1949, Meneely and Kaltreider, 1949; Briscoe, Becklake and Rose, 1951) However, Whitfield and others (1950a) found a larger standard error of about 300 ml

The *mean normal values* as measured by our closed-circuit apparatus for the total lung capacity and its subdivisions are given in Table 8 They are compared with the only other groups of at least 10 normal male subjects which could be found in the literature where the method, age and position of the subject were comparable

Our value for the average functional residual capacity, which is the primary measurement, is higher [illegible] that reported by Aslett and others (1[illegible] pneumoconiosis so that [illegible]

values [illegible]

appreciated

The residual capacity is measured indirectly from the functional residual capacity by the subtraction of the expiratory capacity; when expressed as a percentage of the total lung capacity it shows less variation between normal subjects and is less affected by sex and posture than any other subdivision similarly expressed (Whitfield and others, 1950b). It is, however, closely related to age (Greifenstein and others, 1952, Needham and others, 1954) It shows very good repeatability, and in 50 consecutive cases of pneumoconiosis of varying severity between the ages of 26 and 66 (mean age 45) we obtained duplicate measurements at one sitting with a standard error of a single observa- [illegible] values for paired [illegible] in- [illegible] on [illegible] is ratio of the test in pneumoconiosis is relatively poor [illegible] little change between normal subjects and men with advanced pneumoconiosis

Ventilatory inequality. We have not found the closed-circuit apparatus nearly so satisfactory for estimating mixing efficiency, partly because of instrumental limitations, and also because of the increased complexity of theoretical analysis

TABLE 8

Summary of normal values reported by different authors for the subdivisions of the total lung capacity in adult male subjects using the closed-circuit hydrogen or helium dilution method

Test	Authors subjects			Needham, Rogan and McDonald 1954			Bates and Christie 1950	Briscoe, Becklake and Rose 1951	Whitfield et al 1950 a, b			Aslett, Hart and McMichael 1939			Birath 1944		
	Mean	S.D.	% T.L.C.	Mean	S.D.	% T.L.C.	Mean	Mean	Mean	S.D.	% T.L.C.	Mean	S.D.	% T.L.C.	Mean	S.D.	% T.L.C.
T.L.C.	6·90	0·96	100	6·23	0·83	100	—	6·32	5·74	1·02	100	5·42	0·84	100	6·57	0·61	100
V.C.	4·77	0·75	70·5	4·13	0·73	66·4	—	—	4·00	0·83	69·8	3·8*	0·55	71·0	5·08	0·48	77·3
I.C.	3·20	0·64	46·4	—	—	—	—	—	2·73	0·60	47·8	—	—	—	3·39	—	51·6
R.C.	1·57	0·45	22·8	1·24	0·41	20·0	—	—	1·27	0·47	22·0	1·32	0·30	24·6	1·69	—	25·7
F.R.C.	3·70	0·72	53·6	3·33	0·48	53·4	3·16	3·24	3·02	0·77	52·2	2·92	0·60	53·7	3·18	0·45	48·4
Rd.C.	2·12	0·33	30·8	2·10	0·52	33·8	—	1·57	1·75	0·58	30·2	1·59	0·50	29·0	1·49	0·23	22·7
	40 subjects Ages 23–58 Mean age 44·3			102 subjects Ages 20–70 Mean age 41·3 Vols. expressed at room temp. 17–22° C			27 subjects Ages 17–62 in 2 groups 17 subjects Mean age 27 10 subjects Mean age 53 *Average* F.R.C. same for both groups. Sex not stated.	12 subjects Ages 15–75 Mean age 36	64 subjects Ages 10–70 Mean age not given			64 subjects Ages 19–63 Mean age 38·3 38 subjects under age 39 26 subjects over age 40 *Mean of 66. F.R.C. only corrected for temperature			16 subjects Ages 18–39 Mean age 29·3		

of results in a system in which the concentration of inspired gas is *continually* changing The only index we have found that is easily calculated from the results is the overall index of ventilatory inequality Our mean values for this [illegible]

Needham and others (1954)

We found the standard error of a single observation of the index to be 1 2 per cent units (20 replicate readings on 10 subjects recorded at one sitting) Thus although there was a wide variation in this index between one normal subject and another, the repeatability within a subject was good

The systematic discrepancy between our normal results and those of Bates and Christie is interesting since considerable care was taken to make the apparatus and method of calculation identical A discussion of the difference in normal values and the limitation of the index is given in Part III (p 160)

G OPEN-CIRCUIT SPIROMETRY

[illegible] method of measuring the residual capacity introduced by [illegible]

circuit method

A method of determining the efficiency with which the lung transfers gas from the alveoli to the blood was also required Since preliminary experiments with carbon monoxide, suggested to us by Professor R J W Roughton, had indicated that this gas might be used to measure gas transfer, we decided to combine in one apparatus the measurement of the uptake of both helium and carbon monoxide This allowed simpler and more accurate interrelation of the results

[illegible] the most suitable gases [illegible] ility coefficient in [illegible] pin, 1946), so that [illegible] rapidly absorbed and combines with the blood [illegible] gible back tension provided the *blood concentration remains low Further,* both gases are [illegible] helium by virtue of [illegible] *of absorbing* [illegible]

Apparatus

[illegible] inhaled a constant gas mixture from one of two small spirometers [illegible]

carbon monoxide [illegible]

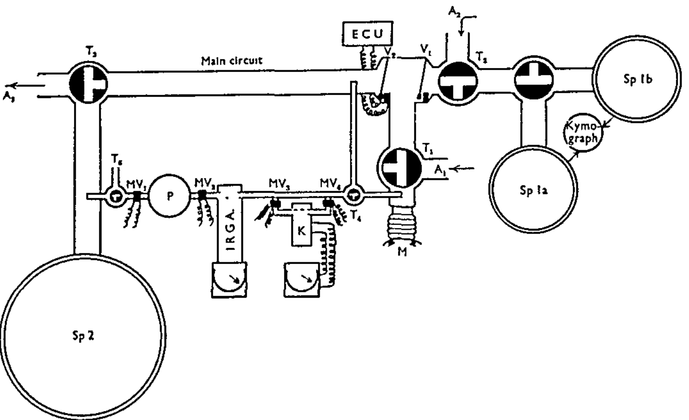


FIG 10 Diagram of open-circuit spirometer system for concurrent estimations of carbon monoxide and helium in the expirate

Fig 10 Diagram of open-circuit spirometer system for concurrent estimations of carbon monoxide and helium in the expirate

of results in a system in which the concentration of *inspired gas is continually* changing The only index we have found that is easily calculated from the results is the overall index of ventilatory inequality Our mean values for this index are given in Table IV, Appendix I (p 232) The mean for our groups N_{25} and N_{35} was 54 4 per cent and for groups N_{45} and N_{55} 47 5 per cent, these are systematically lower than the normal values given by Bates and Christie (1950), who originally described the index, and also those of Briscoe and others (1951) and Needham and others (1954)

We found the standard error of a single observation of the index to be 1 2 per cent units (20 replicate readings on 10 subjects recorded at one sitting) Thus, although there was a wide variation in this index between one normal subject and another, the repeatability within a subject was good

The systematic discrepancy between our normal results and those of Bates and

G OPEN-CIRCUIT SPIROMETRY

The open circuit method of measuring the residual capacity, introduced by Darling, Cournand and Richards (1940), is widely used in the United States (Comroe, 1950) It has the advantage that the inspirate is of constant composition and the mixing efficiency in the lungs can be measured by the rate of gas replacement For this reason, an open circuit helium uptake apparatus was developed as a means of checking the more complex mixing data derived from the closed circuit method

A method of determining the efficiency with which the lung transfers gas from the alveoli to the blood was also required Since preliminary experiments with carbon monoxide, suggested to us by Professor R J W Roughton, had indicated that this gas might be used to measure gas transfer, we decided to combine in one apparatus the measurement of the uptake of both helium and carbon monoxide This allowed simpler and more accurate interrelation of the results

Helium and carbon monoxide were chosen as being the most suitable gases for these measurements, since helium has the lowest solubility coefficient in blood of any inert gas (Lawrence, Looms, Tobias and Turpin, 1946), so that very little passes into the blood, while carbon monoxide is rapidly absorbed and combines with the blood haemoglobin, exerting negligible back tension provided the blood concentration remains low Further, both gases are ... methods helium by virtue of ... of absorbing

Apparatus

... inhaled a constant gas mixture from one of two small spirometers

Calibration of the instrument with standard carbon monoxide mixtures analysed by Graham s iodine pentoxide method to within $\pm 0\ 001$ per cent showed the scale to be slightly non linear The readings were corrected accordingly

Full scale deflexion was given within 2 seconds at the rate of sampling used Thus full response was easily obtained between every fourth expiration at all breathing rates encountered

A general description of the infra red gas analyser is given by Johnston (1947)

Helium katharometer This was similar to the one used on the closed circuit apparatus (p 54) and could be read within 1 per cent of the full scale deflexion To increase the rapidity of response the gas was passed directly over the pair of analyser elements rather than being allowed to reach them by diffusion only as in the closed circuit katharometer Since the analyser elements were rapidly cooled by the stream of gas passing over them the galvanometer had to be shunted to avoid damage to it this was effected automatically by the relay in the electronic control unit the galvanometer being switched back across the bridge as soon as the gas flow ceased The galvanometer then indicated the composition of the gas (about 12 ml) remaining in the katharometer The needle settled within 25 seconds of the start of sampling and thus was satis factory for breathing rates up to 20 respirations per minute At more rapid rates which were infrequent (Table IV Appendix I p 232) error from this cause was found to be slight

Carbon dioxide was not removed from the expirate This gas has a small effect on the katharometer in the opposite sense to helium but this could be determined for each subject at the end of the experiment by observing the difference between the final constant katharometer readings and the full scale reading to which the katharometer was set at the start of the experiment This difference due solely to carbon dioxide was simply added to each katharometer reading a procedure justified by preliminary experiments

Procedure

The procedure itself was very simple A complete estimation from which information on both the efficiency of the intrapulmonary gas mixing and transfer could be obtained took about a quarter of an hour

The dead space (1 33 litres) of the collecting Tissot spirometer and that of the wide bore tubing (4 4 litres) between tap T_3 and the spirometer was first flushed with air T_3 being left open to the aperture A_3 The tubing between the inspiratory spirometers (Sp 1a and 1b) and T_3 was then flushed with and left full of gas mixture

The zero setting of both analysers was checked Next the full deflexion of the analysers was set by turning T_4 so that pure gas mixture could be passed through them and their sensitivity adjusted if necessary During this setting procedure the output from the pump was delivered to the outside through T_6 The analysers were then again brought to zero by flushing them with air and T_6 was closed

After this preliminary adjustment of the apparatus the seated subject put on

after an assistant only had to note the readings of the analysers while the

had been replaced by helium and to which some carbon monoxide was added The gas replacement process in the lungs was followed from the time of its start by automatic analysis of a proportion of the expirate on its way to the collecting spirometer

Main circuit The tap (T_1) close to the mouthpiece (M) enabled the subject to be switched from breathing room air through the opening A_1 to inhaling through the valve V_1 and exhaling through V_2 Gas could come to the inspiratory

The special gas mixture used in the experiments was made up and stored in 100 c ft cylinders and fed from them to the two inspiratory spirometers alternately These were each of the same size and 1 cm movement of the bell

contact was followed by a relay in an electronic control unit (E C U)* so that every fourth expiratory break opened the valves MV_1 and MV_2 on either side of a continuously running pump (P) thereby allowing it to draw a sample of the expired gas from a point very close to the mouthpiece to pass it through an infra red gas analyser (I R G A) which recorded its carbon monoxide content and return it to the collecting spirometer On every alternate impulse from the electronic control unit (that is on every eighth expiration) the valves MV_3 and MV_4 were also opened concurrently with the opening of MV_1 and

katharometer (K) as well

expiration was analysed

ourth and eighth breath

were chosen so that each analyser responded fully before the next sample was taken (see below)

The duration and flow rate of sampling were each independently adjustable, though in practice the output of the pump was fixed at 7 5 litres per minute and the sampling continued for 1 2 seconds from the beginning of every fourth expiration These values were chosen as a compromise to provide satisfactory samples in all subjects

The tap (T_4) enabled the gas mixture to be passed directly through the auto matic analysers before and after every run so that their calibration could be

mixture

ment † The sensitivity was

was

r in

acity

the instrument allowed read

of the analyser tube was 120 ml and that of the rubber tubing leading from the mouthpiece sampling point to the analyser tube 12 ml

* This was designed and made for us by Mr A D Thomas of the P R U

† Obtainable from Howard Grubb Parsons & Co Walter Gate Newcastle-upon Tyne 6 or The Infra Red Development Co Welwyn Garden City Hertfordshire

The concentration of helium in the expirate increases with each breath, at first rapidly and then more slowly, until after about 40 breaths the subject has almost completely washed out the air which was in his lungs and he is exhaling helium in the same concentration as he inhales it. The carbon monoxide concentration in the expirate likewise rises rapidly but only for about 5 breaths, after which it attains a steady value of approximately 50 per cent of that in the inspirate; this constant difference between the results for the two gases represents the uptake of carbon monoxide into the blood.

Unlike the accumulation curves plotted from the closed-circuit data, these helium and carbon monoxide curves represent the increment of change in gas-concentration at each breath. They will be called 'increment' curves to distinguish them. An accumulation curve can be obtained from this open-circuit apparatus either by calculation (p. 70), or by recording the change of concentration, breath by breath, as the expirate accumulates in the collecting spirometer.

Subjects may show a departure from the normal in either or both helium or carbon monoxide curves. The greatest departure in helium curves was found in advanced cases of emphysema, and in the carbon monoxide curves in some unusual cases of fibrosis of the lung (Appendix II, p. 245).

Indices of Inequality of Ventilation (Helium)

In Fig. 12 the helium data from the same normal subject are plotted on the same axes as comparable data from a young subject with advanced clinical and radiological emphysema. The subject with emphysema (No. 200, Appendix II) differs from the normal in two respects: first, he takes about twice as many breaths to wash out his lungs completely with helium mixture; secondly, he rejects a greater concentration of helium in the early breaths. These two differences were characteristic of advanced cases of emphysema; they result mainly from an increase in the functional residual capacity but also from ventilatory inequality in the lung. Five open-circuit indices will be given in this report as an expression of these differences. They are not all equally useful in practice but they contribute to the analysis of the way in which gas-distribution occurs in the lungs and are retained in order to clarify the subject. The indices are as follows:

(1) *Number of breaths to achieve a given percentage of gas replacement.* Since the curves obtained directly from the automatic sampling (Figs. 11 and 12) represent the concentration of helium rejected at each breath as an increment curve, this index from the open-circuit data is not quite the same as that from the closed increment curve. To distinguish the number of breaths for, say, 90 per cent replacement on an increment curve from that on an accumulation curve, the symbol N_{90} will be used instead of N_{90}. In practice, by the 90 or 99 per cent point the N and N′ are numerically nearly the same (see Fig. 13, p. 71). This index has the same limitation as the closed-circuit N for expressing inequality, in that no allowance is made for variation in tidal volume and functional residual capacity in different subjects.

(2) *Relation of increment and accumulation curves as a visual index of inequality of mixing.* The concentrations expressed in the open-circuit increment curves are relative to the inspirate concentration taken as unity (or 100 if expressed as a percentage). Thus, assuming for the moment that a sample representative of the mean expirate concentration is taken, the concentration for each ordinate is numerically equivalent to the mass of helium rejected in one tidal volume. Hence 1 (or 100) minus the quantity rejected is the mass retained in the lung. It is useful to be able to distinguish the 'rejection' (y_r) and 'acceptance' ($1 - y_r$)

operator kept the inspiratory spirometers filled with gas-mixture The experiment was continued until a stable reading on the katharometer showed that gas-replacement in the lungs was complete The patient was switched out of circuit by turning T_1 and the time taken for the experiment was noted on a stop-watch The volume reading of the collecting spirometer was recorded The wide tubing of the main circuit was flushed with air into the collecting spirometer by opening T_3, and a further reading of the spirometer taken

Presentation of Results

In order to explain the indices of gas-mixing and transfer obtained from this apparatus, we must consider a typical example of the results in a normal subject as well as in subjects who showed extreme abnormality in these two aspects of lung function The results from a young normal subject are shown in Fig 11

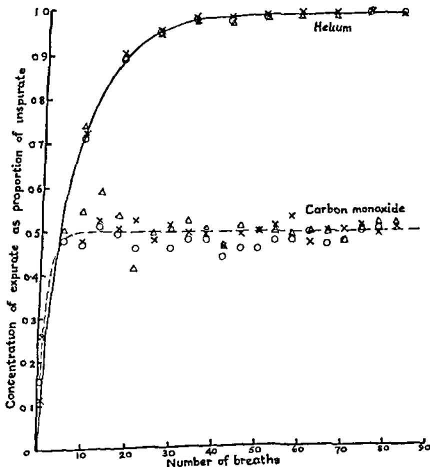


FIG 11 Concentration of carbon monoxide and helium in the expirate sample in relation to the number of breaths after start of inhalation of the gas mixture Normal subject, No 1, aged 28

These are 'increment' curves (see text) The open circles, triangles and crosses are results of replicate determinations

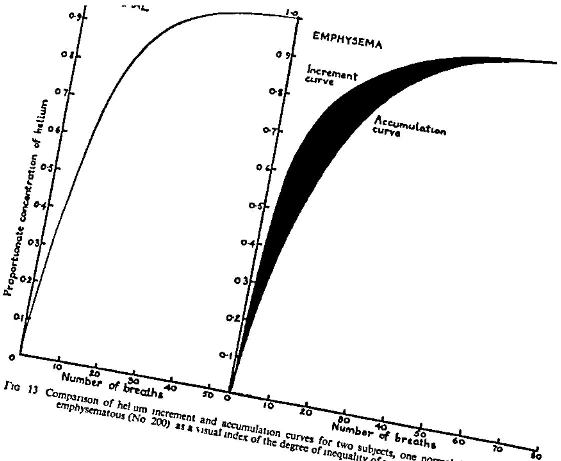


Fig 13 Comparison of helium increment and accumulation curves for two subjects, one normal (No 1) and emphysematous (No 200) as a visual index of the degree of inequality of ventilation in the l

ordinates of the increment curve (these words apply equally well to accumulation curves) See example for breath 9 in Fig 12 The sum of the acceptance ordinates from the first breath to the last represents the functional residual

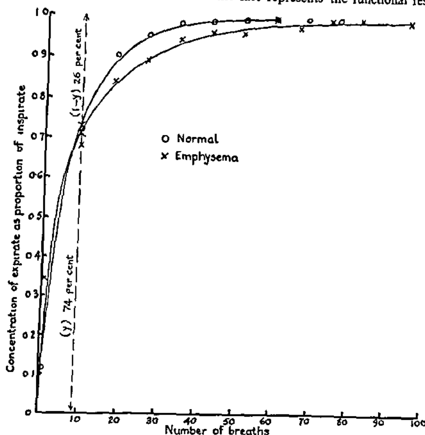


FIG 12 Increment curves representing the change in concentration of helium in the expirate sample related to the number of breaths after the start of inhalation of helium mixture Normal (No 1) and emphysematous (No 200) subjects

... of the effective tidal volume (F/Te) This sum is approximately ... he increment curve (though ... 1 of the acceptance ordinates ... ie number of tidal volumes ... curve can ... *against the* ... ven breath ... of the whole area ... *uformly ventilated, the closer does the* breath represent the average value of the helium accumulated in the lung by that breath In a perfect mixing system, ... and increment curves are the same, on the other ... lation curves gives a good ... entilation ... umulation curves for the ... isual index of ventilatory

residual capacity (which always includes dead-space) and effective tidal volume so that $q = F/(F+Te)$

Again $I_R = 100\ N^{Th}_{90}/N_{90}$ but here the formula implies q′ instead of q so that

$$I_R = -100/N_{90}\log_{10}q' \qquad (7)$$

Because of the post dead space sample automatically taken by our open-circuit apparatus it was possible to calculate I_R directly from the data the sum of the acceptance ordinates was the functional residual capacity in terms of the effective tidal volume, that is F/Te By definition

$$q' = F/(F+Te)$$

$$= F/Te-(F/Te+Te/Te)$$

$$= \sum_{r=0}^{\infty}\left(1-y_r\right)\Big/\left\{1+\sum_{r=0}^{\infty}\left(1-y_r\right)\right\} \qquad (7a)$$

= the sum of the acceptance ordinates divided by their sum increased by unity

(5) *Index of biphasic distribution I_B* When the increment curve is plotted logarithmically against the number of breaths on a linear scale, a linear relationship would be expected if the post-dead space mixing behaved as a single chamber However, this is not so even in some normal subjects and an approximately linear relationship only exists after 10 to 15 breaths (Fig 14) The mixing is therefore behaving essentially in a biphasic manner with one component coming to completion rapidly

The index I_B is the horizontal distance (number of breaths) between the linear part of the logarithmically plotted curve of the increment data and the parallel line to it which passes through the origin (dotted in Fig 14) The nearer the

of the post-dead space mixing from a 'perfect' unitary system, I_B depends on

representation of the acceptance data necessary for calculating I_B is given in Appendix V, p 264

Index of Gas transfer Efficiency (Carbon Monoxide)

Since the rate of carbon monoxide uptake from a constant concentration in

red gas, once the concentration in the expirate was constant (Fig 11, 68)

inequality In the normal subject with little inequality of ventilation the curves nearly coincide in the emphysematous subject the curves deviate due to inequality of ventilation Numerical *indices which measure the inequality of* difference between these curves are given below

In our apparatus the automatic sample was actually a post dead space

effective tidal volume is the tidal volume less a dead space volume equivalent in its effect to that in normal subjects These considerations do not affect the principle of the index illustrated in Fig 13 but are important in defining two of the *remaining indices*

(3) *Overall index I_O* This index can be derived just as in the closed circuit method (p 58) By the 90 per cent replacement point the observed number of breaths is practically identical whether accumulation or increment data are used but the index was made truly comparable and applicable to open-circuit *increment results by using the appropriate model for the theoretical curve* and converting the increment data into accumulation data to obtain the corresponding N_{90} from the N_{90}

The theoretical equation appropriate to the open circuit is a simpler special case of the closed (see Appendix III p 251 eqn 40) the equation being

$$C_{E_r} = 1 - \left(\frac{F}{F+T}\right)^r \qquad (4)$$

The symbol q will be used for the open circuit expansion ratio F/(F+T) to dis

hich also depends on Vm Thus

eqn 2 p 58) *It only differs from*

Q is implicit in the formula and

the index is calculated as in closed circuit equation (3) as

$$I_O = -100/N_{90}\log_{10}q \qquad (5)$$

the ass mption is made that in the perfect mixing 'model

lume mixes intimately with the

the l ng because of the

e part

space

nal subjects the sensitivity of

l differences between normal

on effect of dead space

degree of residual inequality

after allowing for an upper respiratory dead space equivalent in effect to that *in normal subjects This interpretation of the index is justified in* Part III (p 164) As in I_O the index is a comparison of the N_{90} with that of a theoretical perfect model having functional residual capacity and effective tidal volume (Te) the same as that of the subject The equation *appropriate to this model is*

$$C_{E_r} = 1 - \left(\frac{F}{F+Te}\right)^r \qquad (6)$$

The symbol q will be used for the expansion ratio for the equivalent functional

residual capacity (which always includes dead space) and effective tidal volume so that $q' = F/(F+Te)$

Again $I_R = 100\, N_{90}^{T_R}/N_{90}$ but here the formula implies q' instead of q so that

$$I_R = -100/N_{90}\log_{10}q' \qquad (7)$$

Because of the post-dead space sample automatically taken by our open-circuit apparatus it was possible to calculate I_R directly from the data the sum of the acceptance ordinates was the functional residual capacity in terms of the effective tidal volume, that is F/Te By definition

$$q = F/(F+Te)$$

$$= F/Te - (F/Te + Te/Te)$$

$$= \sum_{r=0}^{\infty}\left(1-y_r\right) \Big/ \left(1+\sum_{r=0}^{\infty}\left(1-y_r\right)\right)$$

= the sum of the acceptance ordinates divided by their sum increased by unity (7a)

(5) *Index of biphasic distribution I_B* When the increment curve is plotted logarithmically against the number of breaths on a linear scale, a linear relationship would be expected if the post dead space mixing behaved as a single chamber However, this is not so even in some normal subjects and an approximately linear relationship only exists after 10 to 15 breaths (Fig 14) The mixing is therefore behaving essentially in a biphasic manner with one component coming to completion rapidly

The index I_B is the horizontal distance (number of breaths) between the linear part of the logarithmically plotted curve of the increment data and the parallel line to it which passes through the origin (dotted in Fig 14) The nearer the mixing in the lung after the dead space is to a single hypothetical process the nearer these two lines and the smaller the index Thus, I_B is similar to I_R, but whereas the latter is simply a quantitative expression of the percentage deviation of the post-dead space mixing from a 'perfect' unitary system, I_B depends on the knowledge that gas replacement occurs in two phases, one portion of the lungs being hyperventilated relative to the rest This index is simple, independent of tidal volume and functional residual capacity, and is preferred to all others

Calculation of the indices I_R and I_B In practice, these two indices were derived by plotting the rejection data obtained on the open-circuit apparatus on ordinary centimetre graph paper A convenient method for obtaining the logarithmic representation of the acceptance data necessary for calculating I_B is given in Appendix V p 264

Index of Gas transfer Efficiency (Carbon Monoxide)

Since the rate of carbon monoxide uptake from a constant concentration in the inspirate depends, among other variables, on the magnitude of the ventilation, the results were expressed in terms of the proportion removed from the inspirate, this partly corrects for variation in the subject's ventilation (pp 154, 155) The index used was the percentage of carbon monoxide removed from the inspired gas, once the concentration in the expirate was constant (Fig 11, p 69)

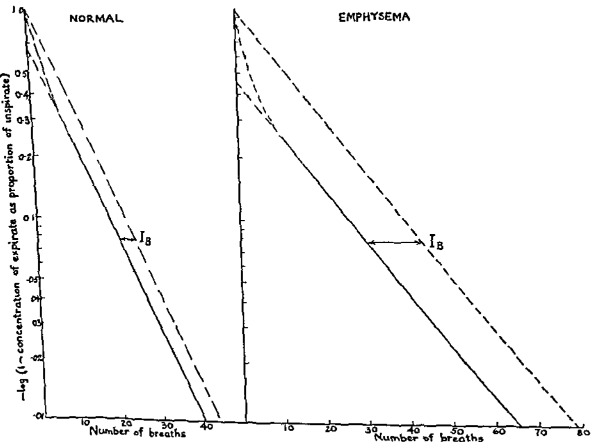


FIG 14 Logarithmic plotting of increment curve (acceptance ordinates 1–y) related to the number of breaths after the start of inhalation of helium mixtures in normal (No 1) and emphysematous (No 200) subjects

Calibration

Preliminary experiments showed that at least a 150 ml sample of gas was required to wash out completely the 120 ml sampling tube of the infra red analyser together with the short length of small bore tubing which led from the mouthpiece to the analysers This volume of gas was obtained by sampling for 1 2 seconds at 7 5 litres per minute We were then able to demonstrate that mixing curves of the mechanical pump ('artificial lung') exactly and repeatedly fitted the curves for perfect mixing calculated from the functional residual capacity and tidal volume (the stroke) of the pump at breathing rates between 9 and 18 per minute The same gas-replacement curves for the pump were obtained for both helium and carbon monoxide, since these two gases are equivalent when no absorption takes place (Fig 15) The sampling was therefore satisfactory when tested on a mechanical model

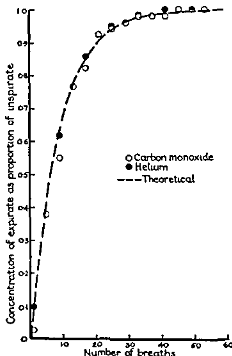


FIG 15 Calibration curves showing gas-replacement in the mechanical pump (artificial lung) measured both by helium and carbon monoxide on the open-circuit apparatus F R C = 3 16 litres T V = 0·54 litres B R. = 18

It was however still necessary to define more precisely what both the helium and carbon monoxide samples represented in terms of the complex changing composition which occurs in man during expiration Thus, pneumotachograms (Fig 16A) were taken of a subject breathing naturally through the apparatus The subject's expiratory flow could be made to pass through the pneumotachograph by turning the tap T_1 (Fig 10, p 65), a record of the breaking of the electrical contact on the expiratory valve (V_2) was taken concurrently The

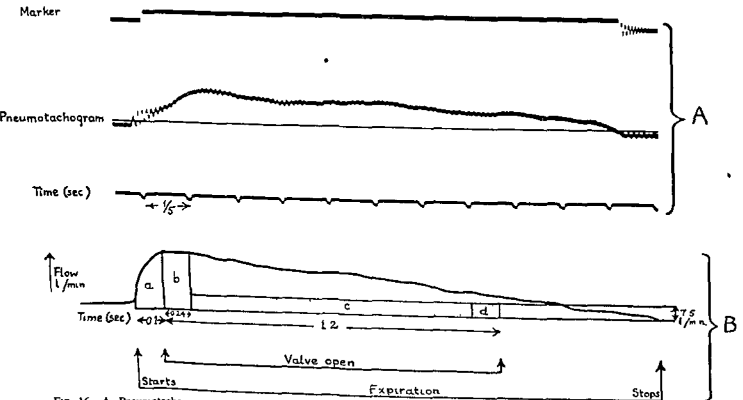


FIG 16 A Pneumotachograms of a normal subject breathing through the open-circuit apparatus The marker indicates time of opening (upward deflexion) and closing of the expiratory valve (V_2) Deflexion above the base line indicates expiratory flow
B Diagram (not to scale) showing relation of helium and carbon monoxide samples to whole of expirate a volume of expirate (not sampled) before electromagnetic valves (MV_1 and MV_2) opened, b, volume of expirate not recorded on I R G A , c, sample of 150 ml drawn through analyser, d, portion representing helium sample

electromagnetic valves controlling the flow through the analyser circuit opened 0 1 second after expiration started, by which time the subject's expiratory flow was well in excess of the 7 5 litres per minute

The nature of the helium and carbon monoxide samples, which were different, can now be deduced

Helium Samples

Since, from Fig 16B, the sample gas-flow stopped at 1 3 seconds after the start of a particular expiration and the volume of the katharometer was only about 12 ml, the gas analysed when the galvanometer was switched into the circuit again was a small 'snap' sample (d) taken at the time of closing of the magnetic valves All the previous part of the sample had passed on into the Tissot spirometer Thus, the points plotted on our mixing curves can be interpreted in relation to the volume time concentration curves for a non-absorbed gas such as nitrogen as measured by Fowler (1948)

Our helium snap sample was a post-dead space sample taken at a constant time after the start of expiration Its relation to dead space is discussed further in Part III (p 164)

Our results are concordant with those of Fowler, Fig 17 shows that the expirate concentration for helium at breath 1, recorded at the 1 3 seconds after the start of exhalation, was higher in emphysematous than normal subjects This was observed in the higher initial rejection in our curves for abnormal subjects (Fig 12, p 70)

Carbon Monoxide Samples

Like the helium ones, the carbon monoxide samples were also post-dead-space, but differed in representing the average concentration of a much larger volume of the 'alveolar' portion of the curve

From the pneumotachogram (Fig 16) it can be seen that the 150 ml sample of gas started to enter the carbon monoxide analyser about $\frac{1}{10}$ second after expiration started Since the analyser had a volume of 120 ml, 30 ml of the initial portion of the sample is not recorded This volume takes 0 24 seconds to flow at the sampling rate of 7 5 litres per minute, so that a volume of expirate equal to the unshaded areas 'a' and 'b' is not sampled This volume of the initial part of the expirate varied between 150 and 190 ml in normal and abnormal subjects Since the absolute carbon monoxide dead-space was found to be about 80 ml (p 189) and the time-volume-concentration curve declines rapidly after this 80 ml, we can be certain that we recorded a post-dead space sample The sample was 'viewed' end on in the infra-red gas analyser so that the average concentration of 120 ml (shaded area 'c') was recorded representing the average concentration in the alveolar gas

With the variation of the respiratory rate found during the main experiment, the end of the sampling period rarely exceeded the time of exhalation In the few cases when it did, it simply meant that any one sample was contaminated by a small quantity of gas in the dead space of the apparatus, but since the contaminant was end-expirate gas, the error was negligible

It will be shown that with this type of post-dead-space sample the expression of carbon monoxide uptake as the proportion of gas removed from the inspirate is relatively independent of the subject's minute volume and of his tidal air

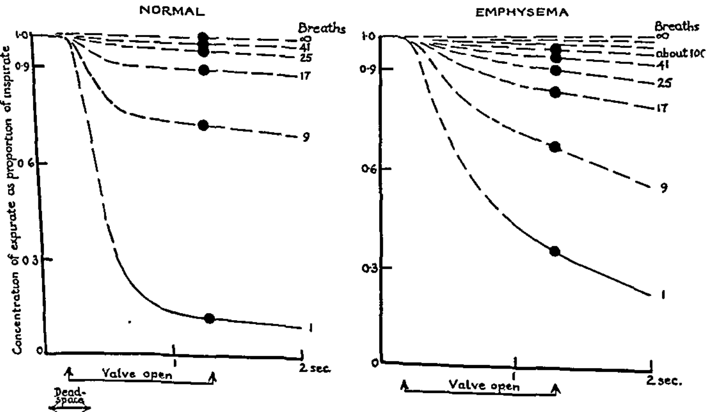


FIG. 17 A theoretical diagram showing relation between the helium samples (●), taken at breaths 1, 9, 17, on the open-circuit apparatus and a time-concentration curve of the expirate in normal and emphysematous subjects The curves for breath 1 are based on those of Fowler (1948) for a single exhalation of the nitrogen in air after breathing pure oxygen, their shape has been assumed to apply to helium curves

Evaluation

Helium Indices

We find the open-circuit method preferable to the closed for measuring 'mixing efficiency' The standard error of a single observation of the indices I_E and I_B found from a small series of replicate observations on 15 normal subjects was 3 83 and 1 3 respectively The mean values for these two indices are given in Table X, Appendix 1 (p 238)

The scatter in normal subjects is much less than in the closed-circuit index I_O, not for instrumental reasons but on account of the nature of the index Both indices I_E and I_B show similar and very good discrimination in pneumoconiosis (D R for I_E 12 09)

Carbon Monoxide Uptake

With rapid infra red gas analysis, the test is simple and requires the minimum co-operation from the subject or skill on the part of the observer The test is rapid since such a short time is required to achieve a constant rate of carbon monoxide removal Even with an inspired gas concentration of 0 3 per cent carbon monoxide, duplicate runs which need only last for about 40 breaths, during which time 10 readings are obtained can be made without producing any symptoms in either normal or abnormal subjects

The standard error of an estimation in 16 normal subjects was 3 94 The mean [illegible]

might be expected pathologically to show a gas transfer defect (p 245) suggests that as a lung function test it may prove useful in other diseases

Our method suggests that normal subjects remove a greater proportion of the carbon monoxide from the inspirate than do the results given by Pace, Consolazio White and Behnke (1946) on 12 normal males, who showed a mean uptake of 41 per cent (S D 4 4) Their scatter is practically identical with ours the systematic difference is almost certainly explained by the difference between the average post-dead space and average overall sample of the expirate taken in the two series The mean values of percentage uptake in a group of 15 normal subjects (ages 19 to 74) reported by Bates (1952) was 50 per cent (S D 7 1)

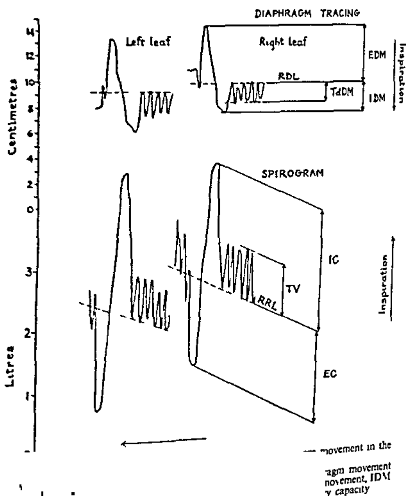
The Use of Helium and Carbon Monoxide Simultaneously

Much is gained by recording the uptake of helium and carbon monoxide concurrently With little trouble to the patient enough information is obtained to calculate the capacity of the lungs their mixing and gas transfer efficiency, [illegible]

development

[illegible]

failed because the curvature of the vertebral column changes during deep inspiration, and also the accurate location of the spine is impossible in some subjects



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y capacity

The standard error of a single radiological measur
iliac crest was 0·53 cm, which is similar to the er
anthropometric measurement by orthodox methods
and Gilson, 1945)

A tracking device is not essential for measuring th
diaphragm provided that the limits are related to a s
the pattern of movement
Vade, 195
servation

position the standi
excursion was 0 59 cm and, when lying 0·61 cm
The values for the resting position of the diaphra
crest in the standing and supine positions are given i

(p 234) together with the values for the total diaphragm movement and expiratory diaphragm movement in the standing position

The diaphragm was systematically higher on the right side in all the normal subjects There was a slight fall in the resting diaphragm level with age but this was only marked in the 55-year age-group The resting level was displaced upwards approximately 2 cm on lying down Both in respect of movement and change in position with posture the left and right diaphragm were similar

The total movement was not appreciably affected either by age or posture, but the expiratory diaphragm movement decreased by about 2 5 cm on lying down A full discussion of the effect of several postures including 45° head down and the lateral positions in normal subjects, has been published previously (Wade and Gilson, 1951), a close relationship between the expiratory diaphragm movement and the expiratory capacity was noted

An extensive search in the literature has revealed few records of measurements of the diaphragmatic movement Our values agree well with the total right diaphragm movement of 6 8 cm ±0 23 recorded on 10 normal subjects by Kaltreider, Fray and Hyde (1938)

In normal subjects the coefficients of variation of the mean diaphragm level and of the mean total diaphragm movement were 12 and 18 per cent respectively In the abnormal groups the reduction of total diaphragm movement was relatively greater than the change of diaphragmatic level The power of discrimination of total diaphragm movement in pneumoconiosis is fair (D R 7 68)

Studies of the pattern of movement of the diaphragm and spirogram recorded synchronously show that considerable changes of diaphragm position can occur without a corresponding flow of air into or out from the chest At the end of deep inspiration the diaphragm lifts but the chest also expands, keeping the volume of the thoracic cavity constant The movement of the diaphragm must therefore not be interpreted directly in terms of changes in lung volume

1 ANTHROPOMETRY

Body measurements were made to check the comparability of the groups selected and to enable a correction to be made for the effects of height or weight or both, when these were shown to be sufficiently closely related to the physiological measurements for the correction to add a useful increase of precision when comparing individuals or groups of subjects (Section IV p 125)

Heights and stem heights were measured to the nearest cm on the scale on the side of the X-ray table Standing height was measured with the subject in stockinged feet, sitting height was recorded seated on a ledge projecting from the X ray table, the thighs horizontal and feet supported

Weights were measured to the nearest lb, in stockings, trousers and shirt

Chest expansion was recorded on some subjects only, with a spring loaded tape which was maintained at a constant tension (240 g) by small spring balances attached to both ends (Morant and Gilson, 1945) A similar device has been shown by Cotterill (1951) to increase the accuracy of measurement of limb-circumference Measurements of chest-circumference were made on maximum expiration and inspiration The level of the dome of the right diaphragm on maximum expiration which was noted at the time of the screening of diaphragm movement was chosen because a subsidiary investigation was being made into the usefulness of an index suggested by Tiffeneau (1949), an account of this has been published elsewhere (Lavenne, Wade, Hugh-Jones

and Gilson, 1953) We are not inclined to place much reliance on the measurement of chest expansion owing to the very poor discrimination (Fig 3, p 42) which we had found in routine observations

Chest diameters Measurements of antero-posterior and lateral diameters in the inspiratory and expiratory positions were recorded using callipers at the level of the xiphisternum In 30 normal subjects the mean expansion in the antero-posterior diameter on deep inspiration was 2 3 cm and 3 1 cm in the lateral diameter Similar values were observed in the most advanced groups of pneumoconiosis and there was a wide scatter in all groups These measurements are therefore not considered further

III. RESULTS

The results given in this section broadly define the relation between disability and radiological change when age is taken into account, and strictly apply only to the 'population' as defined in the experimental plan Their application to other sections of the community of miners or ex-miners, and the use of the results for interpreting the mechanism of different aspects of lung function and for finding the interrelation between the different tests will be considered subsequently (Parts III and IV)

[illegible]

the means of the results for each radiological group, the diagrams have to be interpreted with due regard to this form of presentation Reference will be made to later sections to justify some of the conclusions we draw, and to Appendix I where the tables give the means of the results for each group

1. Clinical Findings

The clinical examination gave the frequency of the more usual signs and symptoms of this disease and the results were of interest for comparison with the impressions which we had gained previously from dealing principally with hospital cases (Table III, p 231)

Breathlessness, the most important symptom, and bronchial spasm are related in detail to the physiological results (see pp 98, 108, 133), while the physical signs in the chest are discussed in relation to the diagnosis of emphysema in Section IV (p. 139)

Cough was present in 80 per cent of men with complicated pneumoconiosis, and in 54 per cent of men with simple pneumoconiosis, it was also present in 46 per cent of miners without pneumoconiosis, where its frequency is strikingly related to age Of the normal group 37 per cent also stated that they usually had a cough, this is rather surprising, although Cochrane, Chapman and Oldham (1951) have shown that the presence of a cough may be unreliably recorded, when completing a pro forma such as we used

Breathlessness preceded the cough in 41 out of 50 of the miners with pneumoconiosis in whom a record was made, this confirms our impression that in this respect the order of appearance of the symptoms is the reverse of that in chronic emphysema when cough usually precedes dyspnoea (Christie, 1951)

Occasional chest pain was reported by 27 per cent and frequent pain by 13 per cent of men with simple pneumoconiosis In complicated pneumoconiosis frequent pains occurred in 24 per cent and this was significantly greater than in simple pneumoconiosis Eight men were orthopnoeic, 3 of them being in the group D_{58}

Of miners with complicated pneumoconiosis 39 per cent reported having at some time coughed up heavily coal-contaminated spit. Haemoptysis, which was usually only of small amount, was often associated with the black sputum and occurred with the same frequency, it was reported in 22 per cent of subjects with either simple or complicated pneumoconiosis This is higher than the frequency (7 per cent) found by Stewart (1948)

Clubbing of the fingers is rare and was only noted on four occasions, all in men in category D Definite cyanosis was also uncommon and only occurred in category D

The blood pressure, which was recorded at the end of the clinical examination on the right arm with the subject supine, showed no notable change with the disease stage Hypertension was uncommon in the men with pneumoconiosis, only one man was rejected on account of it from all the miners seen, whereas there were 4 men in the normal control group in whom the blood pressure exceeded 160/95 and who were rejected from the final analysis partly or solely on this account Our findings therefore differ from those of the Division of Industrial Hygiene, U S Public Health Service (1950), who found a positive association between hypertension (B P >160/100) and the degree of lung fibrosis among 211 men in ferrous foundries in Illinois, and from those of Schilling Goodman and O'Sullivan (1952), who reported a high proportion of subjects with hypertension in operatives exposed to cotton dust

The blood sedimentation rate was done on nearly all subjects (Table III, p 231) The average for the groups was only definitely raised above the commonly accepted upper limit of normal in men with complicated pneumoconiosis and in group 3_{55} (average 14 mm per hour) The absence of a raised sedimentation rate in simple pneumoconiosis was confirmed (Rinsler, 1950) in the underground working population in mine B, who were examined to confirm some of the physiological results Stewart (1948) had previously reported the that the mean sed mentat on rate tends

2. Cardiological Results

(A J Thomas)

Table 9 summarizes the results of the cardiological examinations In the complicated pneumoconiosis group all the subjects except one were examined, but this was not so in the other groups As explained under Methods (p 44), the selection bias was towards those subjects with cardiac abnormality, so that differences between the normal groups and those with pneumoconiosis will probably be minimized rather than exaggerated On the basis of the final assessment shown in Table 9, it is at once apparent that right heart stress is not a feature of simple pneumoconiosis, but that it is a frequent accompaniment of complicated pneumoconiosis, particularly in the oldest age group of category D where half the group shows definite evidence of right heart stress

Auscultation

30 were examined and gave average

le pneumoconiosis, 36 were

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which was thought to be

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TABLE 9

The cardiological assessment of the men examined

Age group	Normal	Normal miner	Simple pneumoconiosis 1/2	Simple pneumoconiosis 3	Complicated pneumoconiosis B	Complicated pneumoconiosis D
25	8—N					
35	5—N	4—N	6—N	7—N	7—N 1—(R)	5—N 1—R
45	7—N	4—N	7—N	6—N 1—AF	4—N 3—(R)	5—N 2—(R) 1—R 1—R
55	6—N	5—N	3—N 2—L 1—N	7—N	8—N 1—N	4—N 4—R 2—R 1—AT

Fluoroscopy

Particular attention was given to detection of prominence of the right ventricular outflow tract

In the groups of normal men and miners the cardioscopic findings were normal in all the 27 men who were screened, 2 of these had heart shadows of the vertical type

In the 31 subjects with simple pneumoconiosis screened, one showed evidence of right ventricular prominence and 4 had normal vertical heart shadows

In the 22 cases in group B, 2 had definite right ventricular prominence and 2 others had borderline signs of prominence of the right ventricle There were a further 6 cases with a vertical heart shape only

From 21 cases examined in group D, 10 had definite evidence of right ventricular prominence and 12 had vertical heart shadows, the findings being coincident in 9 of the cases

It is clear that, as complicated pneumoconiosis advances, a vertical elongated heart shadow becomes much commoner than in normal subjects In addition, prominence of the right ventricle, particularly of its outflow tract, is a feature of the later stages of complicated pneumoconiosis and usually follows the elongation of the heart, but may be present without the other finding The effect of age is not so evident in the cardioscopic findings as it is in the clinical ones

Electrocardiographic Findings

General

The electrocardiographic patterns of the normal men, normal miners and miners with simple disease followed the accepted average of the normal population One normal subject showed marked left ventricular preponderance One man with simple disease, who produced a paroxysm of auricular fibrillation of unknown aetiology, and one normal miner, who was found to have a right bundle-branch block, were rejected from the analysis of the main experiment as a result of the findings

Twenty of the 23 examined in group B had normal standard and chest lead patterns, in the remaining 3 the CR1 chest lead showed an rSr' QRS complex

[illegible]

significant

The more frequent vertical heart pattern in group D tended to lower the R wave in lead I Lead III showed little difference between the groups

TABLE 10

Analysis of leads V1 and V6 giving the mean amplitudes of R and S waves

Lead	Group	R Wave mean (mm)	S D	S Wave mean (mm)	S D
V1	N 25 normals	4 4	(2 1)	12 0	(4 6)
	D 22 abnormals	3 6	(2 4)	13 6	(6 5)
	Difference in means	0 8 (0 2<P<0 3)		1 6 (0 3<P<0 4)	
V6	N 25 normals	15 9	(5 2)	1 1	(1 5)
	D 22 abnormals	10 3	(3 9)	1 9	(1 4)
	Difference in means	5 6 (P<0 001)		0 8 (0 05<P<0 10)	

Table 10 gives the detailed analysis of leads V1 and V6 which best represent the overall chest lead pattern The chief differences between the groups, found in V6, were the reduction in amplitude of the R wave in group D which was significant (P< 001) and the increase in amplitude of the S wave in the same group, which was not, however, statistically significant The full pattern of right ventricular hypertrophy, R>S in V1, was not found, but in 3 cases in group D the R/S ratio was near unity

The V chest lead from the third left intercostal space V2 (3 i c s) was of interest In the 25 normal men examined, the pattern on the lead resembled V2 (Fig 20) In 20 of these subjects r was absent and in the remaining 6 it varied from 1 mm to 4 mm (mean 2 2 mm)

In 22 subjects in group D, r was absent in 13 but was present in the other 9, and varied from 2 mm to 16 mm (mean 6 2 mm) The difference in the overall means, 0·4 mm and 2 5 mm, was significant (0 5>P> 02) The peak of the r' falls on an average 0 07 seconds after the start of the QRS deflexion and

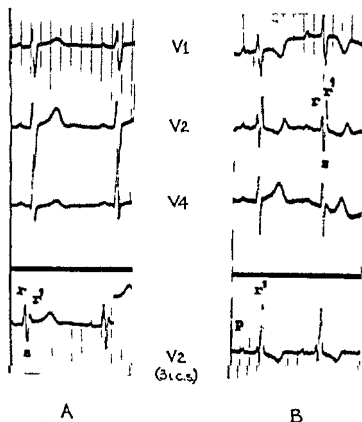


Fig 20 Standard and special [V2 (3 i c.s)] electrocardiograph V leads showing limit of normality (*A*) and extreme abnormality of the r' wave (*B*)

Quantitative measurement of these changes was desirable, so the change in size of the intrinsic deflexion was recorded in the *expiratory and inspiratory* phases, though it will be appreciated that the reciprocal change of R and S robs

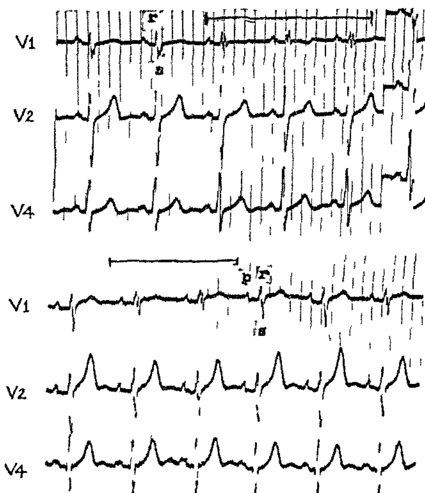


FIG 22 Chest lead electrocardiograms showing variation of pattern with breathing

...ement of some of its significance However, in the 24 subjects

degree in the advanced stages of complicated pneu...
with other signs of right heart change It is well known that there is *respiratory*

variation of the peripheral arterial pressure and several workers have demonstrated changes in the ballisto-cardiogram on respiration, thus it is tempting to say that the electrocardiographic variation results from haemodynamic changes in the right ventricle, due to the pulmonary disease, but this must remain a postulate until further studies are made

The Exercise Test

Heart rate The clinical examination suggested that a rapid heart rate was a frequent feature of the advanced stages of pneumoconiosis The recording of cardiograms at rest and immediately after a standard exercise test allowed a comparison of the resting and exercise rates in the various groups Marked changes were present only in group D In the 25 men examined in groups N and NM, the mean resting pulse rate was 70 per minute (range 60–90) and this mean was raised to 75 per minute immediately after exercise (range 70–110) The few high rates on exercise were in the oldest age group In group D the mean resting heart rate was 86 per minute (range 65–120), the mean rate after exercise was 95 per minute (range 75–140)

In studying individual cases it was noted that the highest resting and exercise rates occurred in those with other evidence of right heart stress and that they were highest in group D_{45} There was a marked increase in heart rate on exercise in those men who had signs of pulmonary heart disease, the increase with this test being of the order of 15 beats per minute A raised resting and exercise pulse rate in a patient with pneumoconiosis is an indication that some heart stress may be present, if no other cause such as intercurrent infection is apparent

T wave The chest leads recording the right ventricle before and after exercise were studied to see if any changes in the ST segments or T waves took place Leads CR1, CR2 and CR4 were analysed

In 19 normal subjects there was an increase in height of the T wave in 17, and a decrease in 2 In the 12 cases thought on clinical and radiological grounds to have some right heart stress, the T wave increased in amplitude in 9, and [illegible]

the presence of right heart stress

3. Physiological Results

It is generally agreed that the main symptom of a ventilatory defect is breathlessness, as opposed to cyanosis which occurs especially when a gas-transfer defect exists Breathlessness on exertion is certainly the main symptom of coalworkers' pneumoconiosis while cyanosis is rare

A VENTILATION

Ventilatory Requirements

The maximum ventilatory capacity of the lungs, by which is meant the limit of output of the lungs as a pair of bellows, must always be greater than the ventilation needed to maintain adequate gaseous exchanges with the blood, if the body's respiratory requirements are to be met in all circumstances In other words, there must always be some 'ventilatory reserve' If the reserve is inadequate, ventilatory failure may occur on exercise, and the subject is forced

Quantitative measurement of these changes was desirable, so the change in size of the intrinsic deflexion was recorded in the expiratory and inspiratory phases, though it will be appreciated that the reciprocal change of R and S robs

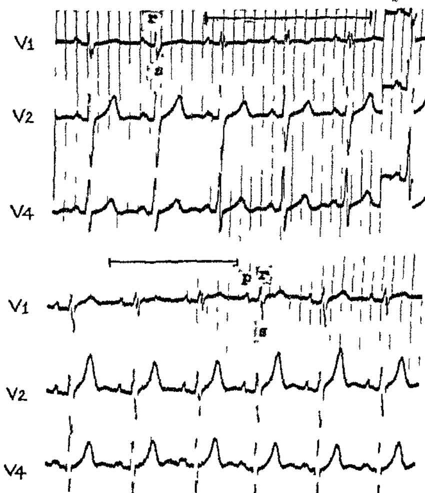


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In 19 normal subjects there was an increase in height of the T wave in 17, and a decrease in 2 In the 12 cases thought on clinical and radiological grounds to have some right heart stress, the T wave increased in amplitude in 9, and and decreased in 3 cases Thus the change in amplitude of the T wave on exercise was of no help in identifying pulmonary heart disease

Similarly, ST segment change was not found to be of any value in assessing the presence of right heart stress

3. Physiological Results

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On Exercise

The ventilatory requirements for a standard amount of exercise (350 kg m per minute for 5 minutes), expressed as the standardized ventilation, are shown in Fig 24 and Table V, p 233, this is an appropriate measure whether the

4 showed a fairly d by age, though there is a slight but definite trend towards increased ventilation with complicated disease, the mean standardized ventilation of those in category D being about 25 per cent greater than that of the normal subjects

In every radiological group, except category B, two or three subjects had an unusually high ventilation on exercise, which was not related to radiological appearance, nor to a history of respiratory disease or to heart failure In group 3 there seems to be a possible relation to age The extreme requirements of the two subjects in group D may be an over estimate since their exercise lasted less than 1½ minutes and in these circumstances standardizing the ventilation may not have been satisfactory

TABLE 11

The frequency with which subjects in different radiological categories performed the full 5 minutes or only shorter times of exercise

Minutes of exercise	No of subjects in radiological category					
	N	NM	1/2	3	B	D
5	30	23	24	22	22	11
4	—	1	—	—	1	—
3	—	—	—	1	—	2
2	—	—	—	—	1	1
1	—	—	—	1	—	8
Total	30	24	24	24	24	22

Table 11 shows that the proportion of subjects in each radiological category who failed to complete the full 5 minutes of exercise increased with disease [illegible] due to breathlessness, but none of those who

[illegible] that there was on [illegible] latory require-

[illegible] *latory Capacity*

and Table V (p [illegible] ventilation is 63 per cent less in men in group D than in the normal [illegible]

Since the maximum voluntary ventilation has been shown usually to provide a better measure of the maximum ventilatory capacity of the lungs than either the ventilatory response to severe exercise or to carbon dioxide inhalation

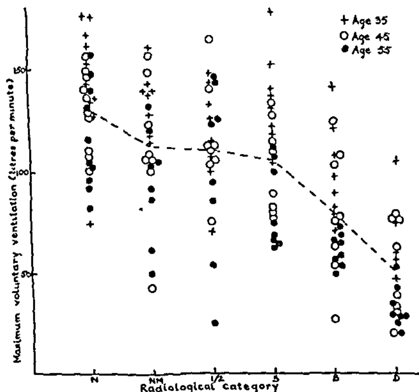


Fig 25 Scatter diagram relating the maximum voluntary ventilation to disease stage and age The line passes through the mean

[illegible]

the degree of simple pneumoconiosis has little effect on the maximum voluntary ventilation In contrast to the standard exercise ventilation, the maximum voluntary ventilation within each radiological category is related to age (Fig. 25) It is clearly shown in Fig 26 that within each radiological category the fall due to age is about the same in absolute units although when expressed as a percentage of the value of the youngest age group, the drop is much greater in category D

Index of Breathlessness

Fig 27 (p 100) shows, in the form of a three-dimensional histogram, the average values for the dyspnoeic index (DI_2) for each age/X ray group on a base which

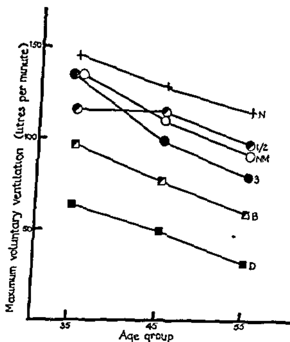


FIG 26 The average maximum voluntary ventilation of each radiological category related to the age group

there is strikingly good agreement Thus, the validity of this dyspnoeic index ... clinical

... there being a greater percentage change from the normal subjects to those in category D The comments below on the relation of X ray change to dyspnoea are in reference to the dyspnoeic index since it is based on measurement rather than ... to be more accurate, but in most cases they

... rage, in each radiological category a steady increase in exertion dyspnoea with advancing age and this effect of age itself increases as the radiological abnormality increases

In each of the three age groups, there is a slight increase in the average dyspnoeic index between the control non miners and the normal miners, the possible causes of this finding, which is perhaps rather surprising, are discussed in Section iv (p 127) On the other hand, there is relatively little increase in dyspnoea with an increasing degree of simple pneumoconiosis except in the oldest men of group 3, who show definitely greater exertion dyspnoea than the normal men of their own age From the relatively flat plateau of dyspnoea in each age group for the groups NM, 1/2 and 3 (other than men in 3_{55}), there is a well marked rise in group B and another rise in group D Thus, the men with complicated pneumoconiosis, especially in category D, in general have severe

exertion dyspnoea Nevertheless, the effect of age is such that the men in group D_{35} are perhaps less disabled than might be expected considering the extreme changes in their chest radiographs (Plate 8)

There seems no doubt that a reasonable estimate of the degree of exertion dyspnoea in a *group* of subjects with coalworkers' pneumoconiosis can be made from the radiological appearance of the chest, provided age is taken into account. However, the scatter about the mean of each age/X-ray group is such (Table V, p 233) that direct assessment of exertion dyspnoea is necessary when assessing individuals

The following general conclusions may be drawn about the breathlessness in pneumoconiosis from these results dealing with the measurement of ventilation

1. In general, men with pneumoconiosis are not breathless while at rest, even when the disease is advanced (except in some of those who are bedridden)

2 The degree of simple pneumoconiosis up to the age of 55 bears very little relation to breathlessness on exertion However, men with category 3 pneumoconiosis are, on the average, more breathless than those men without mining experience Furthermore, age is more important in accentuating the breathlessness in category 3 than in category 1/2 or in normal miners

3 Complicated pneumoconiosis produces severe breathlessness in relation to the radiological disease stage, category D being much worse than category B As with simple pneumoconiosis, age is an important factor, the proportional increase in severity being greatest in the oldest age group examined

4 The exertion dyspnoea is mainly associated with a decrease in the maximum ventilatory power of the lungs, resulting in a lowering of the ventilatory reserve, rather than with an increased ventilatory requirement on exercise

Factors Limiting Ventilatory Capacity

The maximum output of the lungs when considered as a pair of bellows will be controlled by four main factors

1 The forces operating to drive the bellows, that is the muscular forces of the chest wall and diaphragm

2 The stroke volume at maximum output, that is, the tidal volume when performing the maximum ventilation

3 The resistance to the air flow within the bellows, that is, the resistance offered by the bronchial tubes

4 The mechanical resistance within the bellows, that is the resistance due to the viscous and elastic forces within the lung tending to prevent its deformation

A complete analysis of all these factors was not possible when this work was done in 1949, so that we had only an imperfect idea of the underlying defects which caused the reduction in ventilatory capacity in pneumoconiosis Examination of the results of other tests, however, give an indication of likely causes Recently, precise methods have been described for a more complete analysis of the mechanics of breathing (Otis, Fenn and Rahn, 1950, Mead and Whittenberger, 1953, McIlroy and Christie, 1954, Comroe and others, 1955)

The Position and Movement of the Diaphragm

These measurements were made either under resting conditions or after maximum slow inspiration and expiration, so we can gain little information

The reduction in diaphragm movement is accompanied by a change in the resting level of the diaphragm measured from the iliac crest (Fig 30) The mean level in group D is approximately 2 cm below that in the normal subjects The

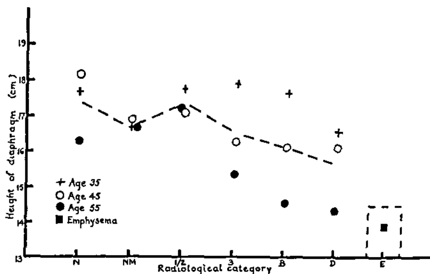


FIG 30 The relation between the resting level of the diaphragm (mean of right and left), measured from the iliac crest with the subject standing, and radiological category, *mean of each age/X ray group Inset shows mean for five cases of advanced* non industrial emphysema

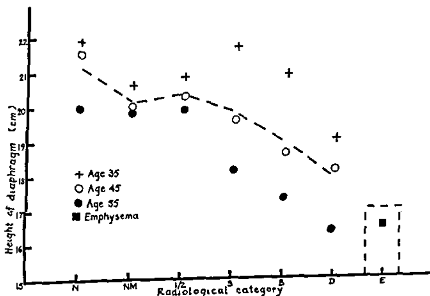
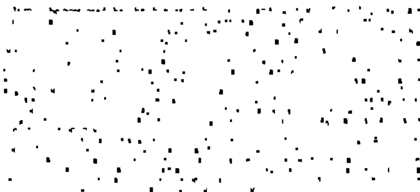


FIG 31 The relation between the level of the diaphragm (mean right and left) on maximum expiration, measured from the iliac crest with the subject standing and radiological category, mean of each age/X ray group Inset shows mean of five cases of advanced non industrial emphysema

level of the diaphragm is much more dependent on age than is its movement and complicated pneumoconiosis seems to enhance the effect of age These changes are all the more marked when the level is recorded in full expiration (Fig 31) and the pattern of change is then very similar to that of the maximum voluntary ventilation (compare Figs 25 and 31) The movement and level of the diaphragm in 5 cases of advanced non industrial emphysema (Appendix II) was found to be similar to that seen in the group D_{45}, and the results are inset into Figs. 29, 30 and 31 for comparison

Inspiratory diaphragm levels are not given because they have no meaning in the absence of simultaneous records of the degree of chest-lifting (p 82)

Our observations on the restriction of movement of the diaphragm in pneumoconiosis confirm those of Bloomfield and others (1936) On the other hand, our finding that the resting level of the diaphragm falls in pneumoconiosis and the few cases of emphysema is at variance with the findings of Whitfield, Smith, Richards, Waterhouse and Arnott (1951), who surprisingly noted no change in the diaphragm level in emphysema From other observations we have made, we think that the method they used, of measuring the level relative to vertebral spines which are less easily localized than the iliac crest and move with the change in thoracic shape in breathing, may have accounted for the difference in the findings



Vital Capacity, Tidal Volume and Breathing Rate

The mean results of vital capacity measurement for different groups are shown in Fig 32 and in Table IX, p 237 A comparison with Fig 26 shows that the pattern of change is similar to that of maximum voluntary ventilation the difference being that, in the 55-year age-groups in categories B and D, the vital capacity is the same as that in the 45-year age-group, while maximum voluntary ventilation decreases proportionately with age Since vital capacity is the maximum stroke of the lung bellows, the similarity in the results suggests that the fall in ventilatory capacity arises partly from a reduction in the size of the bellows

The effect of rate of breathing on

studied i

(1955)

per seco

groups during the maximum voluntary ventilation test was, in fact, remarkably

constant except in group D_{55} where it was reduced, it was little altered by adrenaline Thus, differences in breathing rate are not the cause of the differences in maximum voluntary ventilation

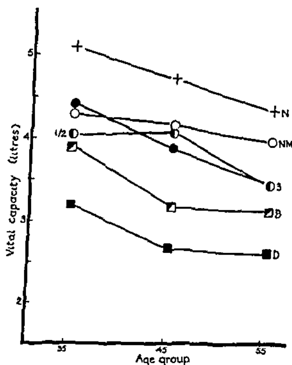


FIG 32 The average vital capacity of each radiological category related to the age-group

TABLE 12

The average number of breaths (to nearest breath) in the 15 seconds of the maximum voluntary ventilation test in the different age/X ray groups, before and after adrenaline

Age group	Average											
	N										D	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
25	15	14										
35	15	14	14	15	13	13	17	17	14	14	14	15
45	14	14	14	13	14	14	14	14	14	14	13	13
55	14	14	13	13	14	14	13	13	14	13	11	11

Table 13 and Fig 33 show the tidal volume as a percentage of the vital capacity used by the subjects in the maximum voluntary ventilation test before and after they received adrenaline This ratio (about 50 per cent in normal

subjects) rose slightly in groups NM and 1/2 and then fell to about 33 per cent in category D Thus, apart from group D_{ss}, whose low maximum ventilation may have been partly due to a slow average breathing rate, it seems that men

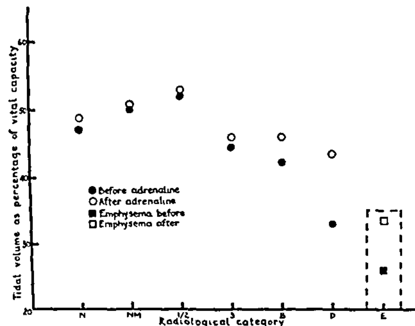


Fig 33 Ratio between the tidal volume used in the maximum voluntary ventilation test, and the vital capacity (open) before and after adrenaline, mean of each radiological group Inset shows the mean for five cases of advanced non industrial emphysema

with complicated pneumoconiosis for some reason use a smaller proportion of their vital capacity than normal men during maximum voluntary ventilation It is interesting to note that the proportion of the vital capacity used in group 3 was similar in all ages, although there was a big difference of 53 litres per minute between the mean maximum voluntary ventilation of the youngest and oldest subjects

Table 13 and Fig 33 include for comparison the average results on the 5 cases of advanced non industrial emphysema Their tidal volume/vital capacity ratio was much reduced, to only 26 per cent, or about half that of the normal subjects This lower proportion agrees with the findings of Baldwin and others (1949b)

Matheson, Spies, Gray and Barnum (1950) made a similar comparison in normal subjects by relating maximum voluntary ventilation to vital capacity assuming a constant optimum rate for producing the maximum voluntary ventilation They found the ratio was 32 8 for young normal subjects (average age 20) For comparison with their figures, this ratio is given for all our groups in Table 14 The ratio is only slightly less in our normal group than the one they quote, it is not appreciably altered by pneumoconiosis, until groups B and D where (as was shown in the more precise comparison of tidal volume

TABLE 13

The tidal volume as a percentage of the vital capacity, used in the maximum voluntary ventilation test, before and after adrenaline

Age group	Tidal volume (% vital capacity) before and after adrenaline in category													
	N		NM		1/2		3		B		D		5 cases of emphysema	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
25	47.5	54.0												
35	46.2	47.8	56.1	51.8	55.6	58.4	44.3	45.5	49.5	54.0	35.5	59.5		
45	48.0	49.0	48.5	51.6	50.0	47.5	46.3	46.5	43.0	49.0	34.8	38.6	26.0	33.4
55	46.5	47.3	45.2	48.6	51.6	52.6	43.3	45.6	34.4	40.2	28.0	32.5		
Mean	47.1	49.5	49.9	50.7	52.4	52.8	44.6	45.9	42.3	47.3	32.8	43.5		

TABLE 14

The ratio of the maximum voluntary ventilation to the vital capacity (open) before and after adrenaline

Age group	Maximum voluntary ventilation (% vital capacity) before and after adrenaline in category. N		NM		1/2		3		B		D		5 cases of emphysema	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
25	29·4	31·3	32·0	32·7	29·0	30·9	31·1	31·8	24·7	28·5	20·9	22·8	13·7	15·0
35	28·3	28·1	26·3	26·6	28·3	29·6	26·1	27·5	24·9	28·9	18·6	20·1		
45	27·8	28·5	23·6	25·4	27·6	28·9	23·9	23·9	19·0	21·5	12·3	14·3		
55	27·3	27·5												
Mean	28·2	28·8	27·3	28·2	28·3	29·8	27·0	27·7	22·9	26·3	17·2	19·1		

used at maximum output, which takes account of rate) men have an unduly small ventilatory capacity for the size of their lungs On the average the older men in all groups tend to use a smaller proportion of their vital capacity doing the maximum voluntary ventilation test

In summary men with simple pneumoconiosis have smaller lung bellows than normal men but can nevertheless maintain a good maximum ventilation Men with complicated pneumoconiosis have very small lung bellows which are also less efficient, their maximum output being disproportionately reduced for their size

Herbst (1928) and Matheson *et al* (1950) have shown that this ratio of the maximum voluntary ventilation to the vital capacity may be used as a rough index of the cause of the reduction of the ventilatory capacity Thus the 'inefficiency' of the small lung bellows in complicated pneumoconiosis might be due to the third of the factors limiting maximum ventilatory capacity (p 99) that is restriction of air flow, either reversible from 'bronchial spasm, or permanent

Bronchial Spasm

The results of giving adrenaline as a test for the presence of spasm (Fig 34 and Table VII, p 235), showed that there was a general improvement in both capacity and maximum voluntary ventilation in all groups including the normal subjects, though the effect was much more evident in the groups of complicated pneumoconiosis in which the mean was materially and significantly increased The effect on the maximum voluntary ventilation was greater than on the vital capacity

The results of the clinical assessment of spasm from the medical history and auscultation of the chest were in agreement with those of the adrenaline test (Figs 34 and 35)

All groups of miners reported some tightness of the chest (Fig 35) In group NM the tightness was usually limited to times when the subject had a cold [illegible] ghtness with advancing radiological [illegible] ltation although quite well related [illegible] method of estimating the presence [illegible] ficant increase of [illegible]

revealed its presence [illegible]

Alternatively adrenaline was also having other effects such as increasing pulmonary vascular tone as suggested by Sheldon and Otis (1951)

The clinical assessments of bronchial spasm from the medical history and from auscultation were made entirely independently of any knowledge of the physiological results It is interesting that there was a greater incidence of a history of tightness of the chest in normal miners than in the normal group

The 'usable portion of the vital capacity used in performing the maximum voluntary ventilation test rose in all groups after adrenaline but the improve ment was greatest in the groups of complicated pneumoconiosis (Fig 33)

These results show that an important factor causing the lowered efficiency of the small lung bellows in complicated pneumoconiosis was reversible spasm Other factors a permanent narrowing of the air-ducts in the lung alteration in compliance of the lung or deficient muscular power in the muscles of the chest and diaphragm may all contribute to impaired ventilatory capacity

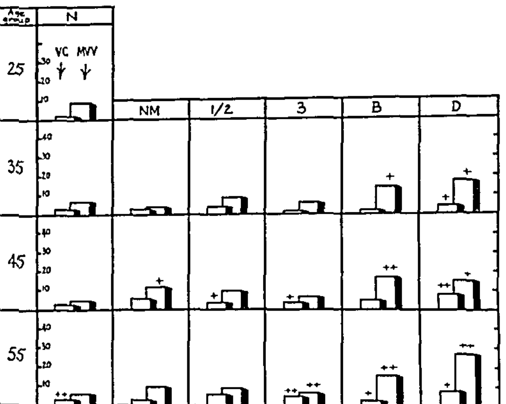


FIG 34 Histogram of the percentage increase in the mean vital capacity (open) and maximum voluntary ventilation after giving adrenaline
Statistical significance at 0·01 % level, +, at 0·001 % level, + +



Fig 35 Histogram of the clinical assessment of 'spasm' by auscultation and from the medical history, group means for the percentage of the maximum possible score.

B. TOTAL LUNG CAPACITY AND ITS SUBDIVISIONS

An attribute of the lungs on which the functions of ventilation, gas-mixing and transfer all depend is their total capacity and the proportion of this normally exchanged by the tidal volume The total lung capacity was measured on the [illegible]

as likely to show gross functional changes It was hoped that they would help to provide a check on the validity of the new tests

The following observations may be made from Fig 36

1. The total lung capacity is practically independent of age in all the groups

2. The total lung capacity is lower in the normal miners than in the normal controls but is uninfluenced by the degree of simple pneumoconiosis, it is lower in the complicated disease than in the simple, but the fact that group D is no lower than group B is of interest (see below)

3 The reduction is predominantly due to a fall in the vital capacity and especially the component inspiratory capacity However, there is also a small reduction in the absolute residual capacity up to group B, but in group D there is then a small increase The general trend of the functional residual capacity is similar to that of the residual capacity but less uniform, a finding which agrees with previous workers' observations that the functional residual capacity is more labile than the residual capacity

4 The small group of cases of advanced non-industrial emphysema show a marked increase of total lung capacity and residual capacity with a reduction of vital capacity The results show that the decreasing total lung capacity and residual capacity of pneumoconiosis are not due to some instrumental error causing low values in subjects with poor ventilatory reserve or mixing deficiency Considering that group D is the only one showing bullous emphysema radiologically (p 5 and Plate 8), it is of interest that this group shows the slight rise in residual and functional residual capacity noted in (3)

In order to allow for variation in total lung capacity the residual capacity is commonly expressed as a percentage of it Fig 37 shows that

1 The residual capacity as a percentage of total lung capacity rises with age in all groups

2 There is a slight upward trend with advancing disease, considerably less than the change with age, except for category D when the percentage increases relatively abruptly This increase occurs in spite of an actual fall in the absolute value of the residual capacity in all groups (except D_{25} and D_{45} and 3_{55}) and results from an even greater concurrent fall in vital capacity

The small alteration of the average percentage residual capacity even with advanced radiological change is interesting (Table VIII gives the mean values for the groups) There were only 19 (16 per cent) miners with a residual capacity of 45 per cent or over out of the whole group of 118 This contrasts sharply with the figures for the 272 miners investigated by Motley and others (1949), of whom 40 per cent had a residual capacity of 45 per cent or over The difference may be due to selection of more disabled individuals in his

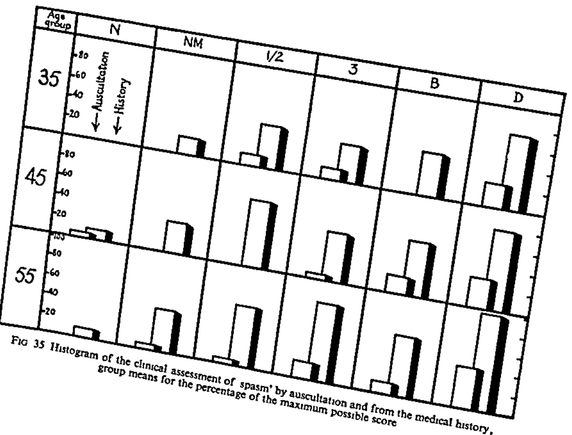


FIG 35 Histogram of the clinical assessment of 'spasm' by auscultation and from the medical history, group means for the percentage of the maximum possible score

B TOTAL LUNG CAPACITY AND ITS SUBDIVISIONS

An attribute of the lungs on which the functions of ventilation, gas-mixing and transfer all depend is their total capacity and the proportion of this normally exchanged by the tidal volume The total lung capacity was measured on the closed-circuit spirometer The average results for the different groups of subjects are shown in Fig 36 and in Table VIII, p 236 In this figure and in those showing results of the gas-distribution and transfer studies, we have included the findings in 5 cases of advanced non industrial emphysema (Appendix II, p 243) They are not necessarily representative of all cases of emphysema, but were selected as likely to show gross functional changes It was hoped that they would help to provide a check on the validity of the new tests

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hospital group,* for Motley comments that percentage residual capacity relates well to disability Age may also be a small factor, the mean age of his 272 miners was approximately 8 years older than our group

Our results show the need for caution in interpretation of a raised residual capacity when expressed as a percentage of total lung capacity Clearly, this *percentage may be raised from two different causes*

1 The absolute value of the residual capacity may be considerably above normal with a normal or even abnormally large total lung capacity

2 The absolute value of the residual capacity may be normal, or even slightly reduced, but the vital capacity may be much more reduced

To confuse these two conditions is to obscure what may be important differences For example, *the 5 cases of non-industrial emphysema are examples* of the group with high absolute and relative residual capacities, whereas the men in group D have much smaller absolute residual capacities but radiologically and almost certainly pathologically have severe emphysema The difficulty in separating these groups in previous reports is that the absolute value of the functional residual capacity and hence the residual capacity is dependent upon the techniques used for its measurement and the posture, age and sex of the subjects Unless an adequate control normal group is given, it is not possible to establish whether there was an absolute increase in either residual capacity or functional residual capacity

C GAS-DISTRIBUTION AND TRANSFER

The results so far have shown that the exertion dyspnoea of pneumoconiosis occurs as the maximum ventilatory capacity of the lungs becomes reduced by the disease But there is some exercise hyperpnoea, which increases with the [illegible] the presence of right heart strain [illegible] that there may be a defect in [illegible] to the major reduction in the capacity of the pulmonary bellows

There are three stages of gas exchange (a) the distribution of each breath within the lungs which determines the relative equality of alveolar ventilation in different lung segments, (b) the gas transfer between the alveoli and blood [illegible]

investigation of gas transfer defects suggest that the pulmonary circulation *cannot be profoundly disturbed by pneumoconiosis until the most advanced* stages Had it been practicable in the conditions of our experiment to use the elaborate procedures of Rossier Bucher and Wiesinger (1947) and Riley and Cournand (1949) to obtain more detailed information on the relation of blood distribution and alveolar perfusion, it is unlikely that the results would have

* [illegible] of all the miners seen as patients at Llandough [illegible]

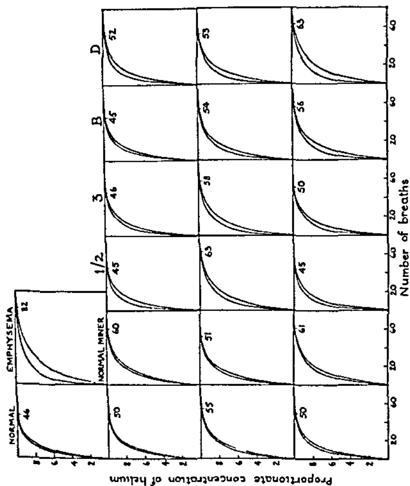


Fig 38 Comparison of open-circuit increment curves (upper) and the corresponding accumulation curves (lower) calculated from them as a visual index, the larger the area between the curves, the greater the inequality of ventilation in the lungs

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[illegible] the distribution of each breath
ventilation
and blood
[illegible] the lungs

These stages may be measured in part by indices already described

We only obtained indirect and scanty evidence on the state of the pulmonary circulation in our subjects from our cardiological studies The results of our investigation of gas transfer defects suggest that the pulmonary circulation cannot be profoundly disturbed by pneumoconiosis until the most advanced [illegible] in the conditions of our experiment to use the [illegible] and Wiesinger (1947) and Riley and [illegible] information on the relation of blood distribution and alveolar perfusion, it is unlikely that the results would have

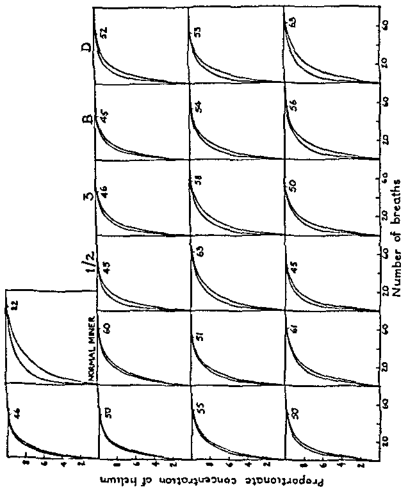


FIG 38 Comparison of open-circuit increment curves (upper) and the corresponding accumulation curves (lower) calculated from them as a visual index, *the larger the area between the curves, the* greater the inequality of ventilation in the lungs

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There are three stages of gas exchange (a) the distribution of each breath within the lungs which determines the relative equality of alveolar ventilation in different lung segments, (b) the gas transfer between the alveoli and blood and (c) the distribution of the blood carrying the gas to and from the lungs These stages may be measured in part by indices already described

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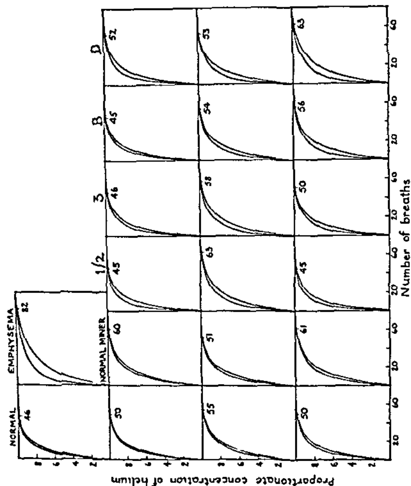


FIG 38 Comparison of open-circuit increment curves (upper) and the corresponding accumulation curves (lower) calculated from them as a visual index, the larger the area between the curves, the greater the inequality of ventilation in the lungs

materially altered our conclusions about the major cause of breathlessness in pneumoconiosis

Gas distribution (helium)

Empirical Indices

Visual index The open circuit increment curves obtained directly during the estimation of gas replacement are compared in Fig 38 with the corresponding

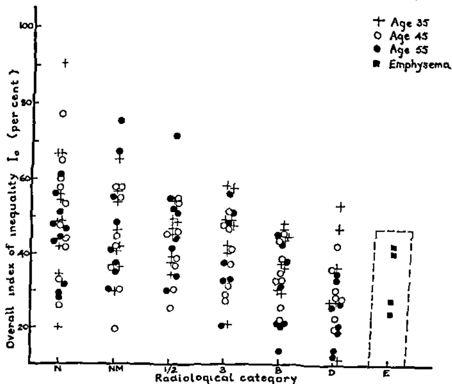


FIG 39 Scatter diagram of the overall index of inequality (I_o) measured on the closed-circuit apparatus related to the radiological category and age Inset shows results for four cases of emphysema

accumulation curves calculated from them Each of the respective curves represents the average values for the group Both curves show a slight tendency to bend further to the right with age and disease stage but in no group is the end point really prolonged as it is in the group of advanced non industrial emphysema The number of breaths to the end point (taken as N_{98}) is mainly a function of the increase in size of the functional residual capacity (which was found not to change much in pneumoconiosis) and a consequent change in the alveolar expansion ratio These changes are associated with increased inequality of ventilation the effect of which is shown by the increasing area between the curves In the young normal subjects the lungs behave almost like a perfectly uniform mixing system and the two curves almost coincide As the degree of pneumoconiosis increases, the divergence between them increases gradually up to a maximum in the 55 year old group D even here the divergence is not nearly as marked as in the emphysema group

Overall index (I_O) This reflects the inequality shown by the visual index The results obtained on the closed-circuit apparatus are given as a scatter diagram in Fig 39 (and in Table IV, p 232)

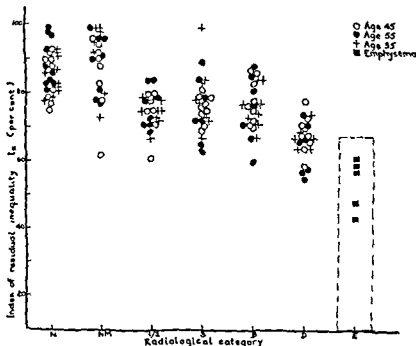


Fig 40 Scatter diagram of the index of residual inequality (I_R) related to radiological category and age Inset shows results for five cases of emphysema

Within each radiological category there is a wide scatter of values and little relation to age but the index on the whole decreases, that is the mixing efficiency becomes impaired, with advance in pneumoconiosis

The index is low (range 25–40 per cent) in the 4 cases* of advanced non-industrial emphysema, though there are a number of subjects even in group N with indices as low as this Thus, the index I_O is very insensitive and does no more than suggest a gradual decrease in mixing efficiency in pneumoconiosis This is the same index as that of Bates and Christie (1950), recorded and calculated in the same way, and the poor differentiation of advanced emphysema cases from normal cases is in contrast to their findings, it is discussed in *Part III* (p 160) The mean values for the groups are shown in Fig 41

The same index calculated from the open-circuit data showed the same wide scatter of results and a comparison of the group means in Fig 42 with those for the closed-circuit in Fig 41 shows that the differentiation of the emphysema group was, if anything, worse, though there was a similar slight impairment of mixing in the pneumoconiosis cases compared with the normal miners and non-miners

* Data were not available in fifth man owing to technical failure.

Analytical Indices (I_R and I_B)

When the effect of the upper respiratory dead-space is allowed for, indices of inequality become more informative (p 163) The results for the two indices

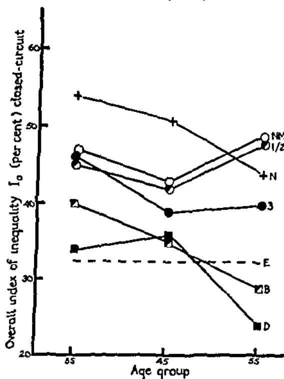


FIG 41 The average values for the closed-circuit index I_o in each radiological group related to age The dotted line shows the average for the index in four cases of emphysema (Mean age, 52)

I_R and I_B are given in Table X (p 238) and shown as a scatter diagram for the index I_R in Fig 40, the diagram for I_B being very similar A comparison of Figs 39 and 40 shows that I_R has much less scatter within the different radiological groups than I_0, the coefficient of variation for the normal subjects of all ages being 7 5 per cent for I_R compared with 28 per cent in the overall index, I_0 Thus, the inequality of mixing in the group of advanced emphysema compared with normal is much greater in terms of the indices I_R and I_B

The relation of these two post dead spaces indices of ventilatory inequality to age and to the radiological disease stage is seen in Figs 43 and 44, where the average value for each experimental group is given

Compared with I_0 both indices I_R and I_B give a somewhat similar picture

with the results for the maximum voluntary ventilation of the lungs (Fig 26) and other tests, (3) with the onset of simple pneumoconiosis (groups 1/2 and 3) there is more inequality in the ventilation within the lungs, but the presence of massive shadows (group B) does not increase this inequality further Once

category D is reached, however, the ventilatory inequality becomes much worse, though even then it is not as severe as in the group of advanced cases of emphysema In this category the large increase in ventilatory inequality at the age

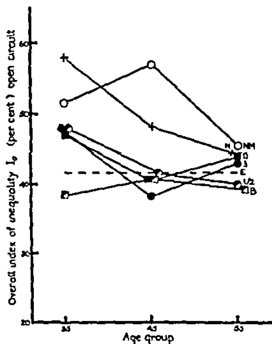


FIG 42 The average values for the open-circuit index I_o for comparison with Fig. 41

of 55 is interesting it is associated with bronchospasm, a marked reduction in maximum voluntary ventilation and with the presence of cor pulmonale

Gas transfer

Carbon Monoxide Uptake

The results are shown as a scatter diagram in Fig 45 (p 122) and also in Table XII (p 240) the average values for each age/X ray group are shown in Fig 46 to make the presentation comparable to that used for the other tests. Two unusual cases of fibrosis of the lungs (Appendix II, p 245) have been included as examples of gas transfer defect, as well as the emphysema group

There appears to be only a slight tendency for the carbon monoxide uptake to be reduced by advancing age, and hardly any change in simple pneumoconiosis There is a significant decrease (about 30 per cent, $P<0{\cdot}001$) in the mean uptake in group D when compared to all the other groups The two cases of fibrosis of the lung show that the uptake can, in fact, be greatly reduced by disease and that the small degree of change in pneumoconiosis does not merely reflect a defect in the test The uptake in the cases of emphysema is similar to that in the severe cases of pneumoconiosis

These results, together with a similar small increase in ventilation on exercise, suggest that gas-transfer deficiency is not a marked feature in simple pneumoconiosis but may contribute to exertion dyspnoea in advanced complicated pneumoconiosis

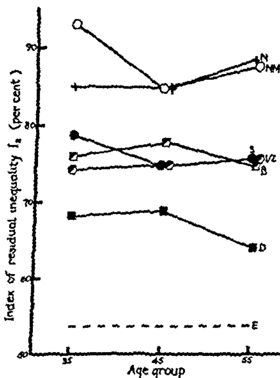


FIG 43 The average value for the index of residual inequality (I_R) for each radiological category related to age The dotted line is the average for the index in five cases of emphysema

Blood Oxygen Saturation

The presence of a low oxygen saturation in the blood may result from a failure of the cardiopulmonary system in two ways:

1. *Impaired gas-transfer across the alveolar membrane* for example, when ... of the membrane

... effectively a shunt
... oxygen
... satura-
... -duced
... oxygen
... the air or increasing the ... 1949b)
... may react
... to the
improved ventilation, others show ... usage is

greater than the improvement effected by the change of ventilation, or because the circulation is failing

It was not practicable to investigate the oxygen saturation on exercise of all subjects in the main experiment The selection led to a bias in all groups towards

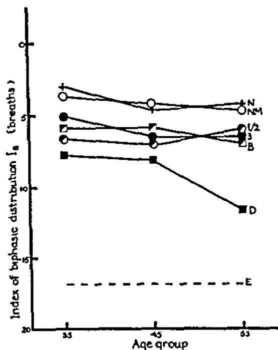


FIG 44 Average values for the index of biphasic distribution (I_B) for each radiological group related to age The dotted line is the average for the index in five cases of emphysema

those who might have been abnormal in respect of oxygen saturation Hence, the conclusions in this section are less representative than those elsewhere

Twelve subjects in group N gave a mean resting value of 94 6 per cent increasing by 1 2 per cent on exercise, this is about 2 per cent lower than the normal figures reported by Lilienthal and Riley (1944) using the same method In groups NM, 1/2 and 3 together, 19 subjects were examined, they had a mean resting saturation of 92 8 per cent which rose to 93 3 per cent after exercise, so they were not different from normal However, there were two subjects, both in group 3_{ii}, who had significantly low resting saturation values of 84 and 85 per cent The evidence we have therefore suggests that in simple pneumoconiosis a lowered oxygen saturation of a serious degree (below 90 per cent) [illegible]

In addition, there were two extra subjects in group D, not included in the analysis of the main experiment (p 31), in whom the saturation fell markedly

These results, together with a similar small increase in ventilation on exercise suggest that gas transfer deficiency is not a marked feature in simple pneumoconiosis but may contribute to exertion dyspnoea in advanced complicated pneumoconiosis

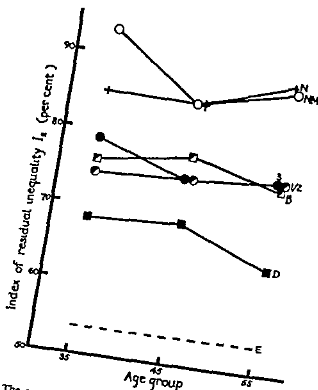


FIG 43 The average value for the index of residual inequality (I_R) for each radiological category related to age The dotted line is the average for the index in five cases of emphysema

Blood Oxygen Saturation

The presence of a low oxygen saturation in the blood may result from a failure of the cardiopulmonary system in two ways

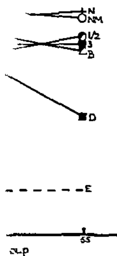
1 Impaired gas transfer across the alveolar membrane for example when a pathological process has led to thickening of the membrane

2 A lack of balance between perfusion and ventilation

When perfusion is much in excess of ventilation there is effectively a shu of desaturated blood through to the arterial side, and increasing the oxyg tension in the inspired air will make no striking difference to the oxygen satur tion in the blood However, if there is normal perfusion but a relatively reduce ventilation, the desaturation may be alleviated either by raising the oxyge tension in the air or increasing the ventilation Baldwin and others (1949b observed that cases of emphysema with oxygen desaturation at rest may react in two ways on exercise some show an increase of saturation due to the improved ventilation, others show a fall because the increased oxygen usage is

reater than the improvement effected by the change of ventilation, or because he circulation is failing.

It was not practicable to investigate the oxygen saturation on exercise of all ubjects in the main experiment. The selection led to a bias in all groups towards



biphasic distribution (I_B) for each ne is the average for the index in five

r respect of oxygen saturation. Hence, representative than those elsewhere ean resting value of 94 6 per cent increas- is about 2 per cent lower than the normal ley (1944) using the same method. In groups were examined, they had a mean resting rose to 93 3 per cent after exercise, so they However, there were two subjects, both in low resting saturation values of 84 and 85 per efore suggests that

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There was ... sug... con... pneumoconiosis ... dyspnoea in advanced complicated

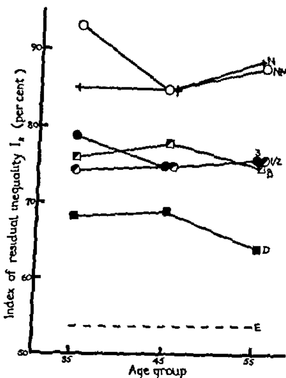


FIG 43 The average value for the index of residual inequality (I_R) for each radiological category related to age The dotted line is the average for the index in five cases of emphysema

Blood Oxygen Saturation

The presence of a low oxygen saturation in the blood may result from a failure of the cardiopulmonary system in two ways:

1 Impaired gas-transfer across the alveolar membrane, for example, when a pathological process has led to thickening of the membrane

2 A lack of balance between perfusion and ventilation

When perfusion is much in excess of ventilation, there is effectively a shunt of desaturated blood through to the arterial side, and increasing the oxygen tension in the ...

... relieved either by raising the oxygen tension in the air or increasing the ventilation Baldwin and others (1949b) observed that cases of emphysema with oxygen desaturation at rest may react in two ways on exercise some show an increase of saturation due to the improved ventilation, others show a fall because the increased oxygen usage is

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It was not practicable to investigate the oxygen saturation on exercise of all subjects in the main experiment The selection led to a bias in all groups towards

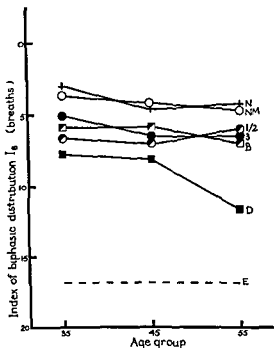


FIG 44 Average values for the index of biphasic distribution (I_B) for each radiological group related to age The dotted line is the average for the index in five cases of emphysema

those who might have been abnormal in respect of oxygen saturation Hence, the conclusions in this section are less representative than those elsewhere

Twelve subjects in group N gave a mean resting value of 94 6 per cent increasing by 1 2 per cent on exercise, this is about 2 per cent lower than the normal figures reported by Lilienthal and Riley (1944) using the same method In groups NM, 1/2 and 3 together, 19 subjects were examined, they had a mean resting saturation of 92 8 per cent which rose to 93 3 per cent after exercise, so they were not different from normal However, there were two subjects, both in [illegible]

groups had a resting saturation of less than 90 per cent Exercise caused a fall in oxygen saturation in 1 out of 11 men in group B, and in 5 out of 14 in group D In addition, there were two extra subjects in group D, not included in the analysis of the main experiment (p 31), in whom the saturation fell markedly

× Age 25
+ Age 35
○ Age 45
● Age 55
■ Emphysema
▲ Fibrosis

Carbon monoxide removed from insp rate (per cent)

0 20 40 60 80

N NM 1/2 3 B D E F

Radiological category

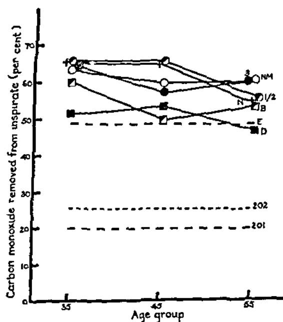


Fig. 46. Average values for the carbon monoxide removed from the inspirate

by 8 and 17 per cent A moderate degree of under saturation at rest there fore may be frequent in complicated pneumoconiosis but is rarely severe (below 80 per cent) This agrees with more numerous observations by Motley

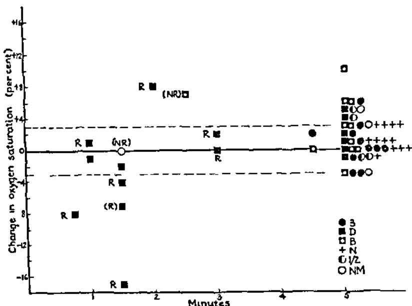


Fig 47 Change in blood oxygen saturation after exercise related to the time of exercise The cardiological assessment is given by the symbol for the radiological group of the subject Values outside the dotted lines indicate a real change of saturation (R) probable abnormality of right heart R definite abnormality of right heart from pulmonary disease

and others (1950a) and with our clinical impression that cyanosis is not a common feature of the disease, though it has been shown that the relation of cyanosis to oxygen saturation is not necessarily close (Comroe and Botelho, 1947)

[illegible]

a mean of 13 8 g per 100 ml

Fig 47 shows the relation of the change of oxygen saturation after exercise to the length of time the subject was able to continue the exercise None of the 4 subjects in whom the saturation fell to a degree which can with confidence be considered outside the error of the method (approx $\pm$ 3 per cent), completed as much as 2 minutes of exercise and they all showed evidence of right heart stress Of the remainder who failed to reach 4 minutes of exercise and showed either a minimal fall or an increase of saturation only one half had evidence of right heart stress Thus the combination of right heart stress and desaturation on exercise is associated with grave disability and in our sample is

limited to group D over the age of 45 Further, our evidence from the study of oxygen saturation suggests, but by no means proves, that in group B pneumoconiosis, low oxygen saturation at rest is usually due to inequality of ventilation (improved by exercise), whereas in category D failure of the circulation is also an important factor

It is of interest that in a few of the grossly disabled subjects in group D, who were severely dyspnoeic on exercise, the ventilation actually continued to increase when they ceased the short period of exercise of which they were capable This phenomenon might be associated with a retention of carbon dioxide, either from circulatory failure or gas exchange

IV. DISCUSSION

1. Criticism of Results

It is essential to be sure that the changes we observed were the consequences of pneumoconiosis and not of other disturbing influences, such as height and weight, bias in selection of the sample, certification, mining experience or employment. We therefore consider these influences before discussing the nature of the functional disturbance in pneumoconiosis shown by our own results and its relation to the radiological appearance of the disease.

A. FACTORS AFFECTING THE SAMPLE

Height and Weight

Since men with different radiological degrees of pneumoconiosis were compared with a control group of normal men balanced for age but not for height and weight, part or whole of the observed differences might have been due to the effect of size. However, changes in size, as measured by stem-height and weight, from one group to another (Table I, p. 229) were small. As would be expected, weight shows a proportionately greater change than height, though both appear on the average to fall with disease. We have made no correction for either variable in presenting the results, an omission which will now be justified.

Table 15 shows the regression relations of stem-height and weight on X-ray category when the latter is measured on a unit scale (Part II, p. 85). Although the height and weight changes were small, their relation to disease was statistically significant, and on the average, there was a drop of about 0.5 cm in stem height and just under 1.5 kg in weight per unit increase in radiological disease.

The relation between tests and size in normal subjects is given in Table 16. The only tests showing a significant relation to height are total lung capacity, vital capacity and functional residual capacity, those showing a significant relation to weight are functional residual capacity, total diaphragm movement and carbon monoxide uptake. From the normal regression relations it is evident that, in general, reduction in height apart from disease could have reduced the total lung capacity by about half a litre (regression coefficient 0.166×3.5 cm change), the vital capacity by about half a litre, and the functional residual capacity by about a third of a litre. The changes we observed (pp. 236, 237) over the whole disease range were generally more than three times as great as these. Thus, even if there were no relation between height and disease stage in the general population of men with pneumoconiosis, the results would still be valid. The survey by Cochrane *et al.* (1952) of the population of a Welsh valley confirms the height disease relation. Our experiment could not show whether men with advanced complicated pneumoconiosis were shorter as a result of the disease, or whether shorter men tend to develop complicated pneumoconiosis.
[illegible]

Although size cannot account for the changes in lung function observed in pneumoconiosis, the effect of size differences between the normal control group

TABLE 15

The relation of stem height and weight to radiological category in each age group expressed as a linear regression

Regression coefficients

Age group	Stem height	Weight
	Coefficient	Coefficient
35	−0 134 ± 0 348	−0 393 ± 0 686
45	−0 599 ± 0 272	−2 267 ± 0 794
55	−0 852 ± 0 246	−1 458 ± 0 626
All	−0 540 ± 0 169	−1 407 ± 0 406

Analysis of variance (all ages)

	Stem height				Weight			
	Degrees of freedom	Sum of squares	Mean square	Significance	Degrees of freedom	Sum of squares	Mean square	Significance
Linear regression	1	128 9272	128 9272	S	1	875 6652	875 6652	S
Deviation	4	93 8125	23 4531	N S	4	553 5756	138 3939	N.S
Difference between categories	5	222 7397	44 5497	S	5	1429 2408	285 8482	S
within categories	142	1740 3076	12 2557		142	10105 7795	71 1675	
Total	147	1963 0473			147	11535·0203		

All regressions are significant (P>0 01) except in the youngest age groups where the regressions though not significant are in the same sense

The arbitrary numerical scale of radiological category used was

Category	N	NM	1/2	3	B	D
Scale units	1	2	3	4	6	8

TABLE 16

The regression coefficients for the principal tests on age and size (stem height and weight) in the normal subjects wherever a statistically significant relationship existed ($P<0.05$)

(The relation to age as well as size is included for completeness In calculating these relations the subjects' actual ages were used)

Test	Related variable	Regression coefficient
T L C	Stem-height	0 166 ±0 037
F R C	Stem height	0 107 ±0 033
	Weight	−0 031 ±0 011
Rd C % T L C	Age	0 020 ±0 009
V C	Age	0 406 ±0·076
	Stem height	0 135 ±0 026
M V V	Age	−0 022 ±0·008
T D M	Age	−1·087 ±0 336
CO Uptake	Weight	0 049 ±0 016
	Weight	0 251 ±0 120
	Age	−0 320 ±0 103

and the normal miners needs further examination The stem-height of the two groups suggested that the normal subjects were not strictly comparable anthropometrically to the miners since there was only about a one in fifteen chance that the differences in height could have arisen from sampling error We must therefore enquire whether the surprisingly large decrease in the ventilatory capacity of the lungs in the normal miners compared with the normal non-miners (p 97) could have been accounted for by the smaller size of the miners From the values in Table 16 we can assess what average change from the non-miner values would be expected in the normal miners from the change in stem-height and weight In Table 17 it is apparent that size change could not have accounted for the decreased ventilatory measurements in the miners

Bias in Selection

Normal Non-miners and Miners

About two thirds of the sample of miners without pneumoconiosis were from coalmine 'A' in the bituminous area of the South Wales coalfield, where there was a low prevalence of certification The men chosen were face-workers, who do the heaviest work underground and, as such, are, if anything, a 'survivor' population selected for fitness Moreover, even within this group, the more disabled men may have been excluded, while the normal non-miners were 'men in the street' not selected for respiratory fitness (p 31), a quarter of the normal control group had a residual capacity of 35 per cent or more Thus the only obvious bias should tend to decrease rather than increase differences in disability between the groups of normal subjects and miners without radiological evidence of pneumoconiosis

In a further confirmatory investigation into this difference of ventilatory capacity the entire population of working miners in the relevant age groups was investigated in coalmine 'B' in another part of the coalfield The results of this

TABLE 17

The difference in stem height and weight of normal miners and non miners, and the average values observed for three ventilatory measurements (T D M, V C, M V V) in normal miners compared with those expected after correcting for the difference in height and weight

Age group	Difference Group N Group NM		T D M (cm)		V C (open) (l)		M V V (l/min)	
	Stem height (cm)	Weight (kg)	* Expected	Observed	† Expected	Observed	‡ Expected	Observed
35	4 0	7 5	5 9	5 9	4 51	4 28	140	135
45	1 5	8 0	6 0	5 3	4 48	4 20	130	112
55	0 5	3 2	6 1	5 5	4 35	4·03	120	94

Notes * Related to weight average change is an increase of 0 05 cm per kg

† Related to stem height and age average change is an increase of 0 135 litres per cm of stem height and a decrease of 0 022 litres per year of age

‡ Unrelated to height or weight but related to age decreasing by 1·09 litres per minute per year of age

The expected values are calculated taking into account the slight differences between the *actual and nominal ages of the groups*

- ~ – ~ Table 18 The s mpler index DI_1 was measured, but
exercise the results are
ice between our normal
ad no radiological evi

dence of pneumoconiosis as estimated by the dyspnoeic index and the maximum voluntary ventilation If anything the difference is slightly greater than in the corresponding group in the main experiment *which might be due to the inclusion* of all miners of the appropriate age groups in pit 'B' and not only face workers as in pit 'A' in the main experiment

We conclude from these results that the working miners in both samples with

sufficient to cause serious disability Further investigations of much larger samples will be required to establish the real importance and cause of the findings

Simple and Complicated Pneumoconiosis

The results suggest that age for age, complicated disease is much more disabling than simple

Although a small minority of the men with pneumoconiosis were chosen from among those attending the hospital (p 31), there were as many in group 3 from this source as in groups B and D, apart from group 3_{55} the men in group 3 showed no more disability than the NM and 1/2 groups If anything the ... towards the less disabled since none

Table I, p 229) Thus,
pattern of the relation

of function and X-ray However, Fig 27 (p 100) showed an unusual increase in the dyspnoeic index in this group 3_{ss} compared with the plateaux for all other miners with simple pneumoconiosis The dotted line B–B′ for group 3_{ss} in Fig 27 shows the average DI_2 for the amalgamated groups of pit 'B' and the main experiment, and represents what we think is a more likely average for this age/X-ray stage

TABLE 18

The relation of the maximum voluntary ventilation (M V V) and dyspnoeic index (DI_1) for the relevant age/X-ray groups of all the underground working miners of mine B to the normal non-mining subjects in the main experiment

Age group	Normal subjects (main experiment)		Miners from mine B					
			Normal		Category 1/2		Category 3	
	M V V (l/min)	DI_1	M V V (l/min)	DI_1	M V V (l/min)	DI_1	M V V (l/min)	DI_1
35	N = 10 145·0 (30 0)	N = 10 17 8 (3 80)	N = 11 104 7* (31 4)	N = 11 31 1 (15 9)	N = 21 113 5 (33 9)	N = 21 28 0 (15 5)	—	—
45	N = 10 130 5 (18 6)	N = 10 18 4 (4 00)	N = 11 107 7 (19 8)	N = 11 25 8 (7 8)	N = 19 108 1 (23 9)	N = 17 27 8 (7 2)	—	—
55	N = 10 118 0 (27 6)	N = 10 22 3 (4 3)	N = 23 80 7 (28 5)	N = 16 39 4 (11 9)	N = 23 91 6 (29 9)	N = 21 35 1 (12 3)	N = 8 93 1 (23 5)	N = 7 36 6 (12 5)

Significance of difference of means between normal subjects and normal miners

	M V V	DI_1
Age 35	$P<0\ 01$	$P<0\ 02$
45	$P<0\ 02$	$P<0\ 02$
55	$P<0\ 02$	$P>0\ 10$

N = number of subjects in each group examined, S D in brackets

* Includes 2 men who were unwell, excluding them mean was 113 7 litres per minute, mean age of this group 1 8 years older than group 1/2

Effect of Certification for Pneumoconiosis

In the main experiment the majority of miners in groups NM and 1/2 were uncertified, whereas the majority of men in groups 3, B and D were certified It is likely that certification selects the more disabled men in any X-ray group, and this might well have upset conclusions reached from our experimental sample However, a survey of the entire population of miners and ex-miners living in one Welsh valley (Cochrane *et al*, 1952) has provided figures showing the proportion of miners certified (Table 19) The age and X ray grouping is not exactly comparable with our sample, but the comparison in the last two columns for the total in the relevant groups shows that our sample was reasonably

TABLE 17

The difference in stem height and weight of normal miners and non miners, and the average values observed for three ventilatory measurements (T D M, V C, M V V) in normal miners compared with those expected after correcting for the difference in height and weight

Age group	Difference Group N–Group NM		T D M (cm)		V C. (open) (l)		M V V (L/min.)	
	Stem height (cm)	Weight (kg)	* Expected	Observed	† Expected	Observed	‡ Expected	Observed
35	4·0	7 5	5 9	5·9	4 51	4 28	140	135
45	1 5	8·0	6 0	5 3	4 48	4 20	130	112
55	0 5	3 2	6 1	5 5	4 35	4·03	120	94

Notes * Related to weight average change is an increase of 0·05 cm per kg.

† Related to stem height and age, average change is an increase of 0·135 litres per cm. of stem height and a decrease of 0·022 litres per year of age

‡ Unrelated to height or weight but related to age decreasing by 1·09 litres per minute per year of age

The expected values are calculated taking into account the slight differences between the actual and nominal ages of the groups

investigation are given in *Table 18* The simpler index, DI_1, was measured, but as the majority of subjects completed the 5 minutes of exercise the results are comparable with DI_2 (see p 48) There is again a difference between our normal *non miner group and the working men in this pit who had no radiological evi* dence of pneumoconiosis as estimated by the dyspnoeic index and the maximum voluntary ventilation If anything, the difference is slightly greater than in the corresponding group in the main experiment, which might be due to the inclusion of all miners of the appropriate age groups in pit 'B' and not only face workers as in pit 'A' in the main experiment

We conclude from these results that the working miners in both samples with [illegible] sufficient to cause serious disability Further investigations of much larg[illegible] *samples will be required to establish the real importance and cause of the findings*

Simple and Complicated Pneumoconiosis

The results suggest that, *age for age, complicated disease is much more* [illegible] niosis were chosen from [illegible] *e as many in group 3* from this source as in groups B and D, apart from g[illegible]up 3_{ss}, the men in group 3 showed no more disability than the NM and 1/2 groups If anything, the selection bias in group D was undoubtedly towards the less disabled since none was bedridden and some had advanced category C X rays (Table I, p 229) Thus, *bias in selection seems most unlikely to have distorted the pattern of the relation*

of function and X ray However, Fig 27 (p 100) showed an unusual increase in the dyspnoeic index in this group 3_{ss} compared with the plateaux for all other miners with simple pneumoconiosis The dotted line B–B for group 3_{ss} in Fig 27 shows the average DI_1 for the amalgamated groups of pit 'B' and the main experiment, and represents what we think is a more likely average for this age/X ray stage

TABLE 18

The relation of the maximum voluntary ventilation (M V V) and dyspnoeic index (DI_1) for the relevant age/X ray groups of all the underground working miners of mine B to the normal non mining subjects in the main experiment

Age group	Normal subjects (main experiment)		Miners from mine B					
			Normal		Category 1/2		Category 3	
	M V V (l /min)	DI_1	M V V (l /min)	DI_1	M V V (l /min)	DI_1	M V V (l /min)	DI_1
35	N = 10 145·0 (30 0)	N = 10 17 8 (3 80)	N = 11 104 7* (31·4)	N = 11 31 1 (15 9)	N = 21 113 5 (33 9)	N = 21 28·0 (15 5)	—	—
45	N = 10 130·5 (18 6)	N = 10 18 4 (4·00)	N = 11 107 7 (19 8)	N = 11 25 8 (7 8)	N = 19 108 1 (23 9)	N = 17 27 8 (7 2)	—	—
55	N = 10 118·0 (27 6)	N = 10 22 3 (4 3)	N = 23 80·7 (28 5)	N = 16 39·4 (11·9)	N = 23 91 6 (29 9)	N = 21 35 1 (12 3)	N = 8 93 1 (23 5)	N = 7 36 6 (12 5)

Significance of difference of means between normal subjects and normal miners

Age	M V V	DI_1
35	$P<0·01$	$P<0·02$
45	$P<0·02$	$P<0·02$
55	$P<0·02$	$P>0·10$

N = number of subjects in each group examined S D in brackets

* Includes 2 men who were unwell excluding them mean was 113 7 litres per minute mean age of this group 1 8 years older than group 1/2.

Effect of Certification for Pneumoconiosis

In the main experiment the majority of miners in groups NM and 1/2 were uncertified whereas the majority of men in groups 3, B and D were certified It is likely that certification selects the more disabled men in any X ray group, and this might well have upset conclusions reached from our experimental sample However a survey of the entire population of miners and ex miners living in one Welsh valley (Cochrane *et al*, 1952) has provided figures showing the proportion of miners certified (Table 19) The age and X ray grouping is not exactly comparable with our sample but the comparison in the last two columns for the total in the relevant groups shows that our sample was reasonably

TABLE 19

The percentage of all miners and ex miners in three towns in one Welsh valley who were certified as having pneumoconiosis in 1950

(Certified primarily applies to the Workmen s Compensation Act (1925) though men diagnosed under the National Insurance (Industrial Injuries) Act (1946) and given more than 5 per cent disability rating are included)

X ray category	Age												Total			Proportion certified in sample in main experiment (all ages)		
	25 34			35–44			45–54			55–64								
	No	Cert	%	No	Cert	%	No	Cert	%	No	Cert	%	No	Cert	%	No	Cert	%
Normal	378	5	1 3	319	4	1 3	366	7	1 9	310	9	2 9	1373	25	1 8	24	1	4
1 and 2	164	18	11 0	209	62	29 7	223	43	19 3	189	44	23 3	785	167	21 3	24	4	17
3 and A	66	30	45 5	90	63	70 0	85	46	54 1	80	46	57 5	321	185	57 6	24	19	80
B, C and D	14	10	71 4	45	33	73 3	52	39	75 0	74	55	74 3	185	137	74 1	46	43	93

representative in groups NM and 1/2, but contained a higher percentage of certified men in the other two groups However, the percentage certified in the B, C and D groups of the population does not represent the true proportion who are certifiable on medical grounds There are administrative reasons for the proportion being low (Hugh-Jones and Fletcher, 1951) Hence (if certification selects for disability) the men in group 3 in our experiment would be the only ones who might be unduly disabled for their radiological stage In fact, however, in ages 35 and 45 there was no difference in breathlessness between these men and those in group 1/2 who were uncertified (Fig 27, p 100) Since it is most improbable that radiological category 3 is actually associated with *less* breathlessness than the earlier stages, we may conclude that in these age-groups certification does not appear to have influenced the results Thus, it is unlikely that the proportion of certified men in our sample was of much importance

Mining Experience and Employment

The proportionate exposure to different types of coal-dust or their mixtures with stone-dust during coalmining experience was distributed in such a way that it will not affect our conclusions Moreover, the work of Hart and Aslett (1942) and Motley (1950) suggests that functional impairment is not related to the type of coal

Practically all subjects (except in groups B_{ss} and D_{ss}) were employed at the time of the experiment However, if the acute effects of dust exposure itself have a deleterious influence on lung function this might partly explain why groups NM and 1/2 were slightly more disabled than the normal non miners Later investigations have shown that this is an unlikely explanation

B GENERAL APPLICATION OF THE RESULTS

The distribution by age and X-ray of over 95 per cent of all miners and ex-miners more than 20 years old, living in a Welsh valley (Cochrane *et al*, 1952), is given in Table 20 It will be seen that within the age range of our experiment age is not closely related to radiological disease-stage

This result is perhaps surprising It appears that of the multiple causes determining the proportion of men in each group, the advance of pneumoconiosis with age seen between 20 and 40 is offset by other factors, such as death from intercurrent infections, between 40 and 60 This lack of close association between age and X-ray in a general population probably means that our results do in fact represent a true picture of the functional significance of a given radiological stage in men between about 30 and 60 years old in South Wales

Table 20 also shows the frequency with which our experimental groups occur in this population, except that groups B, C and D were not separated by Cochrane in the analysis of the survey Under the age of 40, there are relatively few men with complicated disease, and over the age of 50 there are few with category 3 This fits with our being unable to obtain a full quota of men in group D_{ss} and there being few men in group 3_{ss} at mine 'B' Where coalworkers' pneumoconiosis has been observed and investigated in other parts of Britain and elsewhere, the radiological and pathological appearances have been found to be qualitatively the same as those in South Wales (Heppleston, 1951, Cochrane, Davies and Fletcher, 1951, McCallum, 1952) Thus, there is no reason to suppose that the relationship of the radiological appearances to disability would

be grossly different elsewhere unless the X ray change were related to age in a very different manner

Two important limitations in the application of the results remain (i) they *do not* necessarily apply to types of pneumoconiosis other than that in coal workers, for example, pure silicosis, siderosis, *etc*, and (ii) they cannot, even in coalworkers, be extrapolated to other age groups, particularly to men in the sixth and seventh decades

TABLE 20

The frequency of different age/X ray groups in the entire population of miners and ex-miners over 20 years old living in a Welsh valley

Age*	No of miners in category					Total
	Normal	1/2	3	A	BCD	
20–29	*610*	*202*	*32*	*8*	*2*	*854*
30–39	569	333	100	59	53	1114
40–49	571	405	108	74	110	1268
50–59	570	366	56	85	98	1175
60+	615	368	52	106	193	1334
Total	2935	1674	348	332	456	5745

*Age groups between the thicker lines closely approximate to those in the main experiment though in the latter category 3 and a few category A were combined to form group 3 and category B was separated from category D which however also contained a few men in late category C

2 The Disturbances of Lung Function

A MEASUREMENT OF BREATHLESSNESS

We must now consider the relationship of our results to the main symptom of pneumoconiosis—breathlessness on exertion—in order to determine what disturbances of function are chiefly responsible for it To do this we must be able to measure breathlessness, either by attempting a quantitative estimate of the symptom, as we have done in our clinical grading (p 42), or by arbitrarily selecting a particular physiological test as the best index and relating other test results to this standard The latter is the approach used by Motley and others (1949)

South Wales miners, because of the nature of their work and the steep streets which they must surmount going to and from it, often become aware of limitation of their ability for severe exertion earlier than men working in a less hilly district This may account for the good measure of agreement which the two observers attained in grading 92 of the men seen by them both, in individual cases a disagreement was never more than one category (Table I, Appendix I,

p 229) Cochrane, Chapman and Oldham (1951) also reported that this system of subjective grading in miners is not seriously influenced by the observer

This evidence suggests that the method, though crude, is worth using as a standard in the absence of a better one, and we think it preferable to compare objective physiological tests to the subjective grading of breathlessness by an independent observer rather than to guess which test measures breathlessness best

Relation of Clinical Grading to the Physiological Tests

The results in the main experiment (Figs 27 and 28, pp 100, 101) showed there was a good relationship between the dyspnoeic index and clinical grade, but other tests might have been related equally well or better Therefore a comparison was made between clinical grade and a number of other tests maximum voluntary ventilation, percentage residual capacity, carbon monoxide uptake, the index of inequality of gas mixing I_R, total diaphragm movement and standardized ventilation

TABLE 21

The relation between different tests and an independent clinical grading of breathlessness (x)

Test	Regression equation	Correlation coefficient (r)
Maximum voluntary ventilation	$130·6-24·3x$	0·765
Dyspnoeic index (DI_4)	$20·6-1·5x+6·8x^2$	0·830 (quadratic) 0·775 (linear)
Residual capacity (% total lung capacity)	$31·02+3·25x$	0·480
Carbon monoxide uptake	$62·75-3·06x$	0·428
Residual index (I_R)	$79·4-0·44x$	0·528
Total diaphragm movement	$6·07-0·68x$	0·653
Standardized ventilation	$25·60-3·51x+5·97x^2-1·14x^3$	0·635 (cubic) 0·604 (linear)

Table 21 is the result of analyses of variance relating clinical grade to these tests for all the subjects in the main experiment (except group N_{25}), the linear correlation coefficient of breathlessness with dyspnoeic index is the highest ($r = 0·775$), that with maximum voluntary ventilation next ($r = 0·765$), while both these are considerably higher than those for the other tests, though total diaphragm movement and standardized ventilation may be usefully related to breathlessness Thus, we find the dyspnoeic index is better related to breathlessness than any other single test, the relationship is shown in Fig 48

Evidence from Other Workers

Baldwin and others (1948) and Hugh Jones (1952) conclude from a review of the literature that dyspnoea is the main symptom of ventilatory insufficiency and that the degree of dyspnoea is related most closely not to the actual ventilation but to the ratio of this ventilation to the maximum voluntary ventilation

be grossly different elsewhere unless the X ray change were related to age in a very different manner

Two important limitations in the application of the results remain (i) they do not necessarily apply to types of pneumoconiosis other than that in coal workers, for example, pure silicosis, siderosis, etc, and (ii) they cannot even in coalworkers, be extrapolated to other age groups, particularly to men in the sixth and seventh decades

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Although most recent work (Kaltreider and McCann, 1937, Wright, 1942, Baldwin and others, 1948, Warring, 1949) supports the truth of this conclusion, originally proposed by Peabody and emphasized by Harrison (1939), it is still not very generally recognized in clinical medicine, for example, it is not mentioned in a review on 'Dyspnoea' (Christie, 1950)

All the dyspnoeic indices suggested by other observers which have been found to relate well to breathlessness in pneumoconiosis and pulmonary fibrosis are essentially the same, but their quantitative relation to the degree of dyspnoea varies because of differences in the method of performing the tests and in expressing the results However, Motley and his co workers (1948, 1949, 1950), in their study of lung function in coalworkers' pneumoconiosis, did not use a dyspnoeic index of this type and concluded that "the degree of emphysema as measured by expressing residual air as a percentage of total lung volume is a very significant measurement in the evaluation of disability" but did not relate test results to the symptom of breathlessness

In view of the apparent conflict between our conclusions and those of Motley and his co workers, we investigated the point further by comparing maximum voluntary ventilation and residual capacity as a percentage of total lung capacity on a comparable sample

During the last five years we have collected records of clinical grading of dyspnoea, maximum voluntary ventilation and percentage residual capacity on 207 men admitted to our ward All except 16 of these men had radiological evidence of pneumoconiosis and all had some history of dust exposure Of the total, 90 had been admitted at their own doctors' request, and 117 came in at our request, mostly for therapeutic trials In the whole group, the linear correlation coefficients between clinical grade on the one hand and maximum voluntary ventilation and percentage residual capacity on the other were respectively −0 730 and +0 709, compared with −0 765 and +0 480 respectively in the main experiment Thus, in our 'hospital population' of cases of pneumoconiosis, presumably selected on similar grounds to those of Motley and his co-workers, the association between breathlessness and [illegible]

[illegible]

0–2) the maximum voluntary ventilation is rather better related to the clinical grade than percentage residual capacity, but in the more severe grades the [illegible]

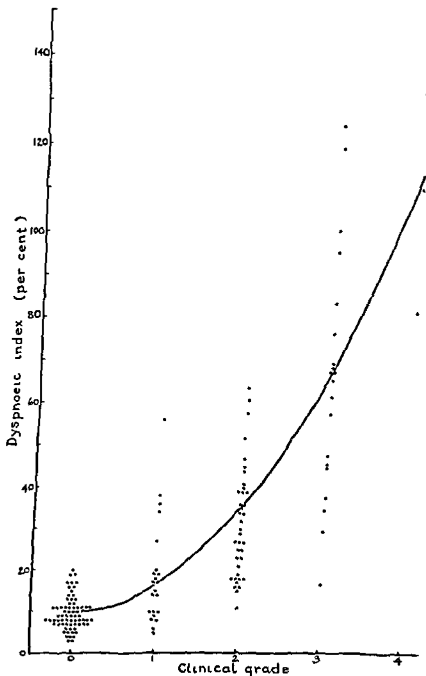


FIG 48 Scatter diagram of dyspnoeic index, DI, related to clinical grading of eathlessness The curve is the quadratic regression line which gave a better fit than the iear one

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This suggests that a fall in the maximum voluntary ventilation is more directly related to the mechanism of the breathlessness than is the rise of percentage residual capacity, and that cases of pneumoconiosis may have definite breathlessness on exertion associated with a reduction in maximum voluntary ventilation, yet no rise in percentage residual capacity

Our evidence does not support the contention that in this disease the residual capacity expressed as a percentage of the total lung volume is as good a measure of breathlessness as the dyspnoeic index

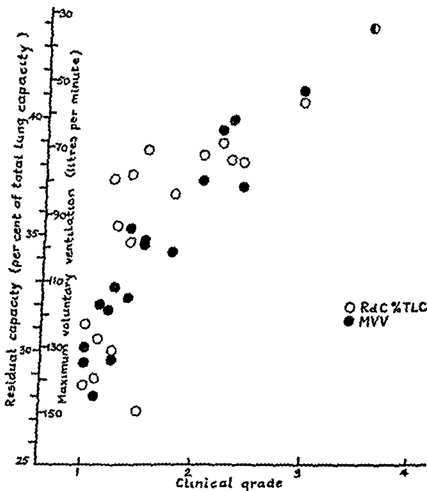


FIG. 49 Scatter diagram of maximum voluntary ventilation and of percentage residual capacity related to clinical grading of breathlessness Means for each age/X ray group (excluding group N_{11})

B CAUSE OF BREATHLESSNESS

We will now consider the variables that may affect the dyspnoeic index Clearly, its value will be altered either by changes in the ventilatory requirement for a given amount of exercise (as measured by the standardized ventilation), or in the maximum ventilatory capacity of the lungs (as measured by the maximum voluntary ventilation) or both

... Fig. 74 (p. 95) that in the exercise test the average standardized ... nd that it was only ... oniosis of the most

advanced degree the average standardized ventilation* was less than 30 per cent above that in the normal group This relatively small increase in ventilation would only account for a 5 per cent units rise in the dyspnoeic index in group D compared with the normal group had the maximum voluntary ventilation remained constant Actually the index rose from an average of about 20 per cent in group N to 80 per cent in group D (see Table V, p 233), so that only about one tenth of the increase was accounted for by the increase in standardized ventilation Thus, factors which may increase the standardized ventilation, such as gas-distribution and transfer and circulatory failure, can probably only play a small part in causing the exertion breathlessness in cases of pneumoconiosis

A small increase of ventilation on exercise in cases of fibrosis and advanced pneumoconiosis was also noted by Kaltreider and McCann (1937), Böhme (1939) Roelsen and Eskildsen (1941) and Wright (1942) However, Zorn (1940), while noting that in normal subjects age has little effect on the ventilatory requirements for moderate exercise and that early silicosis is also without effect found that advanced cases of pure silicosis had an average increase in ventilation of about 50 per cent above the normal, particularly if the masses were in the lower lung fields

Since such a small fraction of the increase in the dyspnoeic index between normals and group D was due to increased ventilation for a given amount of exercise, the principal change must have been a fall in the maximum voluntary ventilation This was shown in Figs 25 and 26 (pp 97, 98) where it was demonstrated that age, too, had an important effect The decrease of maximum voluntary ventilation in absolute units with age is nearly the same in all groups, so that in Fig 26 all the slopes are similar but the proportionate effect of age on the dyspnoeic index is much bigger in group D than in the normal subjects We conclude that in coalworkers' pneumoconiosis the excessive feeling of breathlessness on exertion results primarily from a diminution of the maximum ventilatory capacity of the lungs and only to a relatively small extent from increase in the ventilation required for exercise

Reduction of Ventilatory Capacity

In men with simple pneumoconiosis and in normal miners the small reduction in their maximum ventilation compared with non miners is compatible with the reduction in their vital capacity, though the maximum ventilation of some of the elderly men is slightly smaller than would be expected from the size of their vital capacity

In complicated pneumoconiosis not only is the static volume of the lung bellows further reduced, as measured by the vital capacity, but only a part of this volume can be used in maximum ventilation, so that the output of the bellows is even lower than their size would suggest. In group B this further reduction in output seems almost entirely due to labile bronchospasm restricting air-flow, since the lung output after adrenaline is almost that to be expected from lung size, but in group D besides the very low vital capacity arising from permanent damage in the lung tissue itself, there is an irreversible constriction and distortion of the bronchi so that adrenaline has little effect

In all stages of the disease, but especially the later ones, the muscle forces used to drive the lung bellows become inadequate to overcome the increased

* Omitting the two subjects with S V over 100 both of whom completed less than 1 5 minutes of exercise

forces of airway resistance and change in lung compliance, especially as the diaphragm is lowered and its movement reduced

At the time this work was being done (1949) most attention was being paid to biochemical and gas transfer aspects of lung function Baldwin *et al* (1948) had stated "the measurements and analysis of ventilatory function are in most respects adequate" We cannot now agree with this statement, for our findings in pneumoconiosis showed that it was the *cause* of reduced ventilatory capacity which needed analysis, and we are therefore in agreement with Matheson *et al* (1950) when they said "It would be of material advantage in clinical analysis of respiratory disease if in addition to measuring the degree of reduction in ventilatory capacity the cause of the impairment could likewise be identified" Since then many new techniques have been developed for analysing the mechanics of breathing so that the contribution of changes in airway resistance, tissue viscance, muscle force etc can now be more easily assessed separately (Otis, Fenn and Rahn, 1950, Mead and Whittenberger, 1953, McIlroy and Christie, 1954)

Increase in Ventilatory Requirement

The rise in ventilatory requirement on exercise is sufficiently marked, particularly in the groups of complicated pneumoconiosis, to merit consideration of its origin

Gray (1950) has shown that even in normal individuals no theory satisfactorily accounts for the increase of ventilation on exercise, and that it is necessary to postulate unidentified factors regulating the response of the respiratory centres We only studied arterial oxygen saturation before and after exercise and have no

arterial carbon dioxide tension unaltered) such as Rossier, Bucher ... (1947) observed

Our observations (Figs 43 and 44, pp 120, 121) showed that the degree of inequality of ventilation as revealed by the indices I_R and I_B is on the average relatively slight, and much the same in groups 1/2, 3 and B, but it is more marked in group D However, even in advanced complicated disease the impairment of mixing in the lungs is not nearly as severe as in the cases of advanced emphysema, ... similar average values of standardized ventilation ... e an important cause of ... is supported by Roelsen ... The poor relationships ... irement on exercise may be accounted for by inadequate perfusion in the poorly ventilated areas

Since the indices I_R and I_B seem to be the most sensitive of all our tests of the functional changes associated with emphysema (as a comparison of Figs 43 and 44 with all the other similar figures shows), the above conclusion implies that the ventilatory inequality which results from emphysema does not, *per se*, cause the breathlessness (see p 145) On the other hand, the carbon monoxide uptake, which measures the overall gas transfer efficiency of the lung might be more closely related to the increased ventilation on exercise There was little change in either carbon monoxide uptake or standardized ventilation between the normal group and men with simple pneumoconiosis, but in complicated

pneumoconiosis there was a decrease of carbon monoxide uptake running parallel with the increase of standardized ventilation The summary in the factor analysis of all the changes in pneumoconiosis (Part IV, p 212) shows this almost perfect inverse relationship most clearly It is also of interest that the two cases of unusual pulmonary fibrosis who showed such a striking reduction of carbon monoxide uptake also had high exercise ventilations

Thus, our findings suggest that there is a deficit in overall gas transfer which is associated with increased ventilation, largely limited to complicated pneumoconiosis We differ from Motley and others (1950), who found that the transfer gradient in 160 cases of anthracosilicosis was increased and not correlated with the degree of emphysema In the groups in which we observed diminution of carbon monoxide uptake, the oxygen saturation of the blood was sometimes diminished and evidence of right heart failure was present

Conclusions

We conclude that

1 By far the most important cause of breathlessness in pneumoconiosis is reduction in the ventilatory capacity of the lungs

2 The small increased ventilation required for exercise accentuated the breathlessness, particularly in the later stages of the disease and in the oldest subjects

3 The increased ventilation is but poorly related to the inequality of gas distribution and is mainly due to the same causes as those which impair the uptake of carbon monoxide

4 The evidence of right heart strain shows that the pulmonary circulation is disturbed, this associated with the ventilatory inequality suggests that the gas transfer deficit is the result of a changed ventilation perfusion ratio

C THE ROLE OF EMPHYSEMA

In clinical medicine the word 'emphysema' is commonly used to describe a clinical picture with more or less characteristic history signs and symptoms, but most clinicians find it difficult to define the condition in precise terms Often the diagnosis depends principally on the absence of other causes of breathlessness In this discussion we do not refer to a disease entity but to a functional syndrome, and not merely to a particular clinical syndrome but to a variety of conditions showing functional changes which, although similar are caused by different disease processes producing differing signs and symptoms

The association between pneumoconiosis and emphysema is interesting, since in both the chief symptom is undue breathlessness on exertion Both bullous and focal types of emphysema may be present in pneumoconiosis, and it is therefore natural to enquire whether the breathlessness is attributable to the emphysema (Gough 1947) But the pathological changes in the two diseases (Gough, 1952) are different in their distribution, and this might enable us to distinguish during life corresponding differences in functional disturbance between men who have emphysema as a result of dust exposure from those with emphysema quite unrelated to their occupation The occupation of mining with or without heavy dust exposure might produce or accelerate in susceptible individuals the onset of emphysema without their developing radiological evidence of pneumoconiosis

All methods of diagnosing emphysema are subject to error, and in none can a precise boundary of abnormality be defined which would permit an absol

diagnosis in any but fairly advanced cases Thus no one method can be set up as an absolute measure of emphysema because we are trying to compare

Knott and Christie 1951 Whitfield *et al* 1951 Theodos *et al* 1950 Hurtado *et al* 1934 Baldwin *et al* 1949b) to rationalize the concept of emphysema and to relate the separate entities They have shown that in life there is good agreement between clinical and radiological emphysema only in the most advanced stages when both may correspond quite well with the post mortem findings

functional syndrome of emphysema measured physiologically and not requ ring the presence of particular physical signs We have attempted to assess the severity of this functional syndrome in the subjects in our main experiment the circumstances were not ideal but were adequate to see how the method might be applied

The first consideration is what functional tests should be selected and how they may be combined to measure emphysema We believe that the use of a single test to study extreme cases is of great value in isolating a particular ... of the spectrum

(p 202) shows that in no test are the results wholly unrelated ... tests In so doing we are using essentially the same process as that employed by

can be measured It ought therefore to be possible to do ...

... minant analysis

... s to be related ...
the main experiment was planned to study ... and not emphysema ... emphysema Therefore we do not consider ... nant func... e analysis
might take if given larger groups

Table 22 shows the discriminant ratios of the individual tests when used for comparing the normal subjects in the 55 year age group with the group of men with advanced non industrial emphysema (average age 54) The discriminant function was calculated from the four best tests and the inclusion of any of the other tests did not improve it In deriving the function certain important assumptions have been made

1 That the differences between test results in group N_{55} and the non industrial ... functional syndrome of emphysema
... ined represents the functional changes
... is assumption cannot be fully justified

but the cases were selected as typical both clinically and physiologically from many cases attending a special clinic for emphysema run by Professor R V Christie, who has made an intensive study of this subject for many years Further, the principal differences between the two groups showed themselves in results of tests which are reported by the majority of other observers to show abnormality in emphysema

3 That by selecting a group at opposite ends of the scale of abnormality we have the best measure of intermediate stages and that test results lie on a linear scale

These assumptions may not be strictly true but in the absence of any independent measure of the lesser degrees of emphysema they appear not unreasonable as a first approximation

TABLE 22

Discriminant ratios between group N_{ss} and the non industrial emphysema group for different tests

Test	D R
Index of inequality of mixing (I_B)	9 060
Maximum voluntary ventilation	6 177
Residual capacity (% total lung capacity)	5 054
Functional residual capacity	4 513
Total diaphragmatic movement	3 317
Vital capacity	3 170
Diaphragm level	2 131
Carbon monoxide uptake	1 362
Standardized ventilation	1 325

Our choice of tests may well be criticized We do not claim that the particular discriminant function we have derived is necessarily the best combination of tests There are other investigations for example the sensitivity of the subject to an increase of carbon dioxide in inspired air (Scott 1920 Donald and Christie 1949) which might be included The method might have its greatest use in the study of the prevalence of emphysema in a community or a group applying for compensation The circumstances of its use would therefore also influence the choice of tests

There is also an important property of discriminant analysis which has a bearing on the choice of tests The analysis makes the most efficient use of the information for separation of groups into normal and abnormal however if the results of two tests are very highly correlated—even though they are tests of distinct functions—using them both will not improve the efficiency of the discriminant analysis Conversely two tests which are poorly correlated may add to the efficiency of the analysis even if they are each rather insensitive

Our use of discriminant analysis for assessment of emphysema is no more than a preliminary trial of a method using the material available to us

We have calculated this index of functional emphysema for the means of the groups in the main experiment The results are seen in Fig 50 which shows

1 A progressive decrease of the index (indicating increase of emphysema) from the normal group to men with complicated pneumoconiosis group D

diagnosis in any but fairly advanced cases Thus, no one method can be set up as an absolute measure of emphysema because we are trying to compare dissimilar but overlapping entities, namely clinical, radiological, physiological (functional), and, after death, pathological 'emphysema'

Attempts have been made by workers (Christie, 1934, 1944, Fletcher, 1952, Knott and Christie, 1951, Whitfield *et al*, 1951, Theodos *et al*, 1950, Hurtado *et al*, 1934, Baldwin *et al*, 1949b) to rationalize the concept of emphysema and to relate the separate entities They have shown that in life there is good agreement between clinical and radiological emphysema only in the most advanced stages when both may correspond quite well with the post mortem findings

functional syndrome of emphysema measured physiologically and not requiring the presence of particular physical signs We have attempted to assess the severity of this functional syndrome in the subjects in our main experiment, the circumstances were not ideal but were adequate to see how the method might be applied

The first consideration is what functional tests should be selected and how they may be combined to measure emphysema We believe that the use of a single test to study extreme cases is of great value in isolating a particular functional defect, but that it is restrictive because the continuity of the spectrum from normality to advanced disease and the multiplicity of functional disturbance is obscured We prefer to rely on multiple tests since the factor analysis [illegible] to all other

emphysema from a weighting of all his observations But the physiological [illegible] are quantitative and relatively independent of the observer, and the weighting can be measured It ought therefore to be possible to do better than the clinician in a limited set of circumstances

[illegible] analysis

and one

nd those

with emphysema in relation to the scatter within the groups [illegible] purpose, however, it is essential to have large groups if the result is to be reliable Since the main experiment was planned to study pneumoconiosis and not emphysema, we only have 5 cases of advanced emphysema Therefore we do not consider

[illegible] of the particular discriminant func-

ble of the form the analysis

ividual tests when used for

comparing the normal subjects in the 55-year age group with the group of men with advanced non industrial emphysema (average age 54) The discriminant function was calculated from the four best tests, and the inclusion of any of the other tests did not improve it In deriving the function certain important assumptions have been made

1 That the differences between test results in group N_{55} and the non industrial [illegible] are due to the functional syndrome of emphysema

but the cases were selected as typical both clinically and physiologically from many cases attending a special clinic for emphysema run by Professor R V Christie, who has made an intensive study of this subject for many years Further, the principal differences between the two groups showed themselves in results of tests which are reported by the majority of other observers to show abnormality in emphysema

3 That, by selecting a group at opposite ends of the scale of abnormality, we have the best measure of intermediate stages, and that test results lie on a linear scale

These assumptions may not be strictly true, but, in the absence of any independent measure of the lesser degrees of emphysema, they appear not unreasonable as a first approximation

TABLE 22

Discriminant ratios between group N_{ss} and the non industrial emphysema group for different tests

Test	D R
Index of inequality of mixing (I_B)	9·060
Maximum voluntary ventilation	6 177
Residual capacity (% total lung capacity)	5·054
Functional residual capacity	4 513
Total diaphragmatic movement	3 317
Vital capacity	3 170
Diaphragm level	2 131
Carbon monoxide uptake	1 362
Standardized ventilation	1 325

Our choice of tests may well be criticized We do not claim that the particular discriminant function we have derived is necessarily the best combination of tests There are other investigations for example, the sensitivity of the subject to an increase of carbon dioxide in inspired air (Scott, 1920, Donald and Christie, 1949) which might be included The method might have its greatest use in the study of the prevalence of emphysema in a community or a group applying for compensation The circumstances of its use would therefore also influence the choice of tests

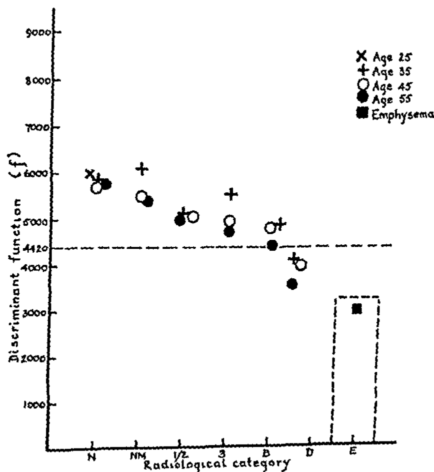
There is also an important property of discriminant analysis which has a bearing on the choice of tests The analysis makes the most efficient use of the information for separation of groups into normal and abnormal, however, if the results of two tests are very highly correlated—even though they are tests of distinct functions—using them both will not improve the efficiency of the discriminant analysis Conversely two tests which are poorly correlated may add to the efficiency of the analysis even if they are each rather insensitive

Our use of discriminant analysis for assessment of emphysema is no more than a preliminary trial of a method using the material available to us

We have calculated this index of functional emphysema for the means of the groups in the main experiment The results are seen in Fig 50 which shows

1 A progressive decrease of the index (indicating increase of emphy-from the normal group to men with complicated pneumoconiosis, group

2. That only men in group D have on the average undoubted emphysema, i.e. are all below the dotted line which is half-way between the average value for normal subjects aged 55 and that for the 5 cases of advanced emphysema on



the downward trend of the

of emphysema

roup have on the average

the same group, except

in the normal group where the index shows very little scatter with age

as a percentage of the total lung capacity is

between the groups, the oldest men in the normal group being on the same level in the figure as the young men with category D complicated pneumoconiosis This index therefore shows poor discrimination of emphysema

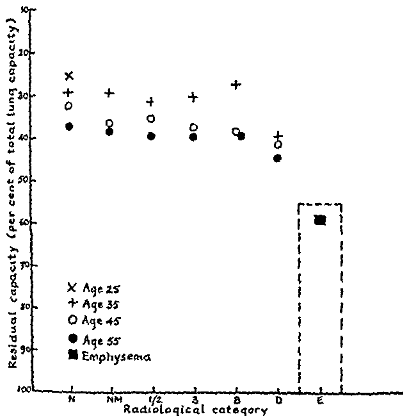


Fig 51 The residual capacity as a percentage of the total lung capacity for each age/X ray group as an index of emphysema for comparison with Fig. 50 group means

An independent clinical assessment of emphysema by one observer using the seven physical signs* was also made on the subjects in the main experiment Although we know (Fletcher 1952) that the error between different observers attempting to elicit physical signs in the chest is large a comparison of clinical and physiological assessment of emphysema is of some interest and the comparison is given in Fig 52 where the clinical evidence is presented as a percentage of the total possible marks in each group This index of emphysema also has a poor discriminating power in pneumoconiosis

* r

To summarize although there is no satisfactory single test for emphysem the use of a combination of several tests in a discriminant function makes possible to obtain *an index which is* useful for the objective assessment of tl

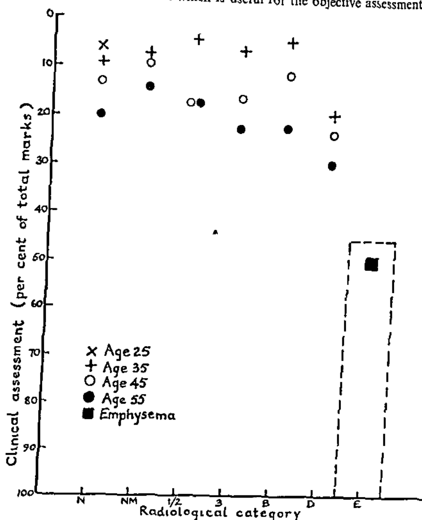


FIG 52 Clinical assessment of the degree of emphysema for each age/X ray group from the combination of seven physical signs expressed as a percentage of total marks on an arbitrary scale, for comparison with Fig 50

degree of functional emphysema in a group or individual Calculating this index for the groups of miners in the main experiment showed that men with category D complicated pneumoconiosis have as a rule severe functional emphysema Men with simple pneumoconiosis also have more evidence of emphysema than miners without pneumoconiosis, the increase is itself not significant statistically but the general trend suggests that it does not arise by chance

Having attempted a definition of emphysema in functional terms and illustrated its measurement in pneumoconiosis, we must now consider the part it plays in causing breathlessness

The index of ventilatory inequality is so much more discriminating in emphysema than the other three tests that it alone separates the cases of advanced emphysema from the group of normal subjects of the same age almost as well as the whole discriminant function does This in no way invalidates the principle of using a discriminant function, had the samples been larger the addition of the other tests would probably have made a significant contribution

The correlation of the clinical grade of breathlessness with the index of ventilatory inequality was lower (r = 0 53, Table 21, p 133), than with the maximum voluntary ventilation (r=0 77), but is still fairly high, this is mostly explained by the intercorrelation of the two tests (r=0 48) The partial correlation of the clinical grade of breathlessness with the index of ventilatory inequality when the maximum voluntary ventilation is held constant is only 0 28, but is highly significant.

Heppleston (1953) has suggested that the disability in simple pneumoconiosis is caused by the increase in dead-space produced by the focal emphysema At first sight the inequality of ventilation in groups 1/2, 3 and B compared with N and NM seen in Fig 43 might be taken as indicating the presence of this increased dead-space If this is so, it is difficult to explain why there is no age relationship to inequality of ventilation whereas focal emphysema is both more common and more severe in elderly subjects We suggest that the clue lies in impairment of elasticity of the lung which increases with age This reduction in the retractility of the lung would bring into prominence focal emphysema in the elderly when the lung section was prepared by the inflation technique of Gough and Wentworth (1949) The same physical changes producing the altered retractility may be the cause of the reduced ventilatory capacity and consequent disability

Thus, we think it possible that the inequality of ventilation in simple pneumoconiosis may be caused by focal emphysema, but it is not itself the cause of the disability

In conclusion, it has been shown, using a functional definition of the syndrome of emphysema, that the latter occurs in simple, and the early stages of complicated, pneumoconiosis, but is only severe in category D The best single functional measure of the presence of emphysema namely ventilatory inequality, is not of itself important in causing the breathlessness in pneumoconiosis But the same pathological process which produces the upset gas-distribution appears to alter the physical properties of the lung, reducing the maximum ventilatory capacity and causing the exertion dyspnoea, though the latter effect is enhanced by age whereas the ventilatory inequality is not In category D the severe change in gas-distribution results from bullous emphysema only in this obvious stage of emphysema can there be said to be good agreement between the clinical, radiological, physiological and pathological diagnosis of it

D THE RELATION OF THE RADIOGRAPH TO BREATHLESSNESS

In Simple Pneumoconiosis

Fig 27 (p 100) showed that within the range of simple pneumoconiosis there was no average increase in breathlessness on exertion with increase in radiological abnormality On the other hand the increase in breathlessness that normally occurs with age was accentuated so that whatever the d... pneumoconiosis, old men were proportionately more ...

compared with normal non miners of equivalent ages * Thus, it is a man's age rather than the radiological degree of simple pneumoconiosis which is important in predicting his disability This generalization *does not apply to* other information derived from the X-ray, such as diaphragm level, the shape of the cardiac shadow etc , and is only known to be true within the age range of about 30–60 years In general, the amount of breathlessness resulting from simple pneumoconiosis is slight, though there is about a 30 per cent variation around the mean dyspnoeic index particularly *in the oldest subjects, so that* some elderly individuals are severely disabled

In Complicated Pneumoconiosis

In contrast to the simple disease, the breathlessness in complicated pneumoconiosis is nearly always severe, increases with the radiological abnormality and is augmented even more by age Thus, on the average, if a man's X ray shows complicated pneumoconiosis, his disability may be estimated reasonably well by taking both age and radiological category into account The diaphragm level on inspiration and expiration and the shape of the heart may give further information of value, a long, thin heart shadow, rather than a large one, especially when accompanied by a large outflow tract, is suggestive but not diagnostic of right heart strain

It is not surprising, remembering the scatter about the mean that other workers who used earlier systems of X ray classification in which the group with massive consolidation was not subdivided and who neglected the effect of age, have been unable to demonstrate the true functional significance of the radiograph

In Miners with Pneumoconiosis of less than Category 1

Fig 27 and Table 18 (p 129) showed that the degree of breathlessness for each age was approximately the same whether a working miner had radiographic evidence of simple pneumoconiosis or not The breathlessness in the normal group, compared with the non miners, could not be explained on the grounds of bias in selecting the sample (p 127) It is natural to ask whether the miners' radiographs were *truly normal, but this is difficult since there is an infinite* gradation of degree of abnormality and the classification of radiographs is a subjective procedure Films which we classify as category 1 have so little abnormality that several radiologists with whom we have discussed *them* ... and the Pneumoconiosis Panels of ... nize category 1 for official ... our experiment had been classified by four experienced readers in the P R U as having less abnormality than category 1, so that we can *confidently state that they would generally* be regarded as showing no evidence of pneumoconiosis

... n the

of coalworkers' pneumoconiosis picked out only ...

* The slope of the regression lines predicting DI_1 from X ray category in simple pneumoconiosis increased significantly *($0\,1<P<0\,5$) with increase of age*

† One of the normal subjects so selected was found on re-examination of the industrial history to have worked in a dusty briquette factory

17 of the 24 normal miners as showing very early radiological changes More-over, when the average dyspnoeic index of the miners chosen as being truly normal was compared with the remainder, it was actually lower Thus, the miners with no definite radiographic pneumoconiosis had breathlessness of a similar degree in relation to age as those with simple pneumoconiosis

Further investigation, on much larger and more truly representative samples, would be necessary before it could be definitely established that miners without pneumoconiosis are usually more breathless for their age than workers in other heavy industries It is always possible that repeated dust exposure might reduce the ventilatory capacity, even when dust is not retained near the terminal bronchioles in sufficient quantity to cause radiological pneumoconiosis The average disability of the normal miners was slight but because of the scatter about the mean, the results do raise the issue of whether seriously disabled elderly miners, without definite radiographic evidence of pneumoconiosis, should be considered eligible for compensation (see below)

The Prevention of Disability by Periodic Examination

Simple pneumoconiosis only progresses as such while there is a continuation of dust inhalation (p 3), and more recent data (Roach, 1953) show that the radiographic degree of simple pneumoconiosis bears a good relation to the total dosage of dust which has been inhaled In contrast massive fibrosis, which only arises in the presence of a considerable degree of simple pneumoconiosis (at least category 2), progresses in the absence of further dust inhalation, though at a varying rate Hence, if dust suppression is adequate and category 2 never reached before old age, little disability from dust retention will occur

The rate of increase in disability may be very steep once massive fibrosis starts, because the subject may as it were ascend diagonally up the disability steps in Fig 27 from the near corner to the far, and it is essential that dust control should be adequate and the risk of miners contracting massive fibrosis reduced to a minimum Because disability shows no very close relation to the degree of simple pneumoconiosis, periodic medical examination theoretically provides a system which can ensure the adequacy of dust control and the prevention of a large amount of seriously disabling pneumoconiosis (Cochrane Fletcher, Gilson and Hugh Jones, 1951)

3. The Relevance of the Results to Compensation

Our results have shown that the main disability from pneumoconiosis, namely excessive breathlessness on exertion cannot be distinguished by functional tests from breathlessness caused by chronic non industrial pulmonary disease Any scheme which separates industrial injury benefit from sickness benefit leads to a most difficult decision when an attempt is made to allocate the proportion of the breathlessness in an individual caused by industrial exposure In the National Insurance (Industrial Injuries) Act (1946) such an allocation is attempted, under its regulations there are two separate issues in relation to disability benefit for pneumoconiosis first diagnosis, 'has this man got pneumoconiosis within the meaning of the Act?', secondly disability assessment, 'to what extent is the man disabled and what proportion of his disability is due to pneumoconiosis?' Some of our results are relevant to these two issues

PART III. FURTHER INTERPRETATION OF PHYSIOLOGICAL RESULTS

THE use of helium and carbon monoxide simultaneously to measure gas distribution and transfer was the only test we used which was new The meaning and physiological significance of the results from it are examined in this Section They are more easily understood if the general theory of the process of gas mixing and transfer in the lungs is first discussed

1. General Theory of Gas-uptake

It is a commonplace that breathing consists of an intermittent ventilatory 'wash-out' of the lungs, whereby the ambient air is mixed with the gas in the alveoli, and a continuous process of gas transfer to and from the blood by diffusion across the alveolar membrane Numerous authors have attempted mathematical descriptions of this whole breathing process, and these have been summarized in an excellent critical review by Kety (1951) The discussion in this chapter is developed from his analysis Kety states "it is necessary that an aggregation of millions of separate processes occurring at microscopic levels in the lung or in a tissue (are) represented by a single average process taking place uniformly and simultaneously if there is to be any hope of mathematical treatment " The necessary assumptions limit the direct applicability of these theoretical concepts, though as generalizations they are very useful in understanding the processes of mixing and transfer

which

niform

ediate

When the inspired concentration of the gas is taken as unity, the alveolar concentration (C_A) of any inert gas* may be represented as a function of time (t) by the equation

$$C_A = A_1e^{-k_1t} - A_2e^{-k_2t} \qquad (8)$$

The constants A_1, A_2 k_1 and k_2, as shown by Kety, are functions of the alveolar volume of the lungs (V_A) (which is approximately equal to the functional residual capacity), the *alveolar ventilation, the tidal volume* the pulmonary blood flow and the solubility coefficient (λ) of the particular inert gas† There are two exponential terms in this equation, the first of which represents the

blood

chemical change in the body
in the blood is therefore
ion is proportional to the

defines the
1 by 1 ml of liquid after
partition coefficient of the gas between
partial pressure The values for λ for
od they are almost identical with those

for water

simple model, they refer to *normal subjects* at *constant* barometric pressure so that, unless otherwise stated, they are those for the respective gas tensions and the 100 per cent equilibrium line is when lung and blood *gas tensions are* the same, also, unless otherwise stated, the temperature, ventilation, tidal volume, functional residual capacity, pulmonary blood flow and blood pH are all assumed constant

Consider the gas phase the helium curve (which is a theoretical curve on the assumption of perfect mixing but closely approximates to that in normal subjects) lies to the left, and the curves for gases of increasing *solubility, such as nitrous oxide* ($\lambda = 0\ 47$) and acetylene ($\lambda = 0\ 8$), (which are theoretical curves derived by Kety from the general equation (8)), bend further to the right and show a sharper inflexion The initial *rapid rise of* concentration of these gases in the alveoli is less steep than that of helium since some absorption is taking place and less gas is therefore rejected in the expirate, the subsequent progressive slow rise represents the time taken in saturating the blood tissue mass, so that some interval elapses before the expired concentration (C_E) taken in the simple model as equal to the alveolar concentration (C_A), equals the inspired concentration (C_I) Deviations from *the theoretical curve are now more complex they represent, first, the inequality* of gas mixin [illegible] from the simple *postulate of* [illegible] takes place, [illegible] the lag between the gas being taken up from the lungs and being returned to them as blood arrives from different parts of the body Nevertheless, Kety (1951) finds that the general equation ' although inexact can be used to describe the uptake of gases of different solubility which it does rather faithfully especially in the early phases of saturation"

Now, *consider the blood phase for the inert gases the curves representing* the rise of concentration in the blood are theoretically identical with those *representing* the rise of tension, and are mirror images of the rise of con centration (and therefore of tension) in the alveoli Thus, the helium rise in the blood, expressed as a percentage of its equilibrium value, must occur very quickly, although the absolute concentration at equilibrium would, of course, be very low, while the nitrous oxide and acetylene curves rise more slowly In practice, the blood *and gas phase curves may not rise quite to the* [illegible] from the skin Such a [illegible] hnke and

Carbon Monoxide

[illegible] longer applies [illegible] the [illegible] nple, [illegible] and [illegible] that [illegible] ntra- [illegible] lood, [illegible] hat is [illegible] trous

what happens, and the dotted line in Fig [illegible] oxide curve which he obtained experimentally when hyperventilaton was followed by quiet breathing It will be seen that there is a short phase after

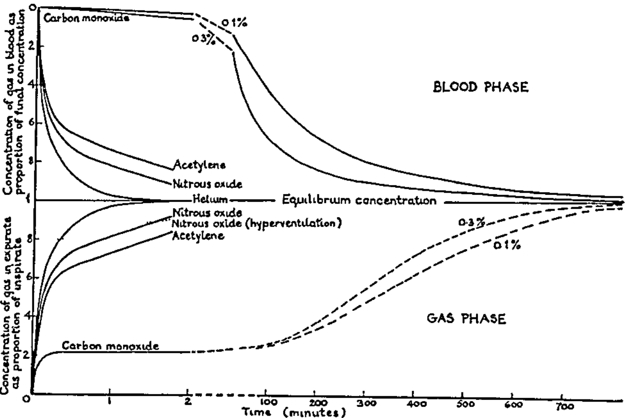


FIG 53 The change in concentration with time of the gas in the lungs and in the blood for some gases of different solubilities and for carbon monoxide.

inflexion when the curve was actually horizontal (representing uptake into the blood with zero back-tension), before the blood recirculated Then, as the blood tension rose, the expirate concentration also rose since the rate of uptake decreased as equilibrium was gradually approached

Now, the diffusion of carbon monoxide from alveoli to the blood follows the general diffusion law so that

$$M_{CO} = K_{CO}(P_A - P_a), \qquad (12)$$

where the rate of diffusion across the alveolar membrane (M_{CO}) depends on its diffusion constant for carbon monoxide (K_{CO}) and the difference between the gas tension in the alveoli (P_A) and that in the alveolar capillaries (P_a) Because of the shape of the carbon monoxide haemoglobin dissociation curve, the arterial tension is effectively zero for some time after the start of inhalation, although the arterial concentration (Ca) is rising continuously as absorption takes place Assuming K_{CO} is approximately constant in normal subjects, the absolute rate of uptake is then proportional to the tension of the alveolar gas Thus, in Fig 53 the carbon monoxide curve (measured on one of our normal subjects) shows an initial phase in which the proportion of gas in the expirate rises This phase represents the time of mixing between the ambient and alveolar gas, though, as for nitrous oxide, absorption is going on concurrently, so that the curve deviates from the helium curve There is then a horizontal plateau of constant (and effectively zero) back-tension in the blood, in which the rate of uptake is constant, and hence the portion of carbon monoxide in the expirate also remains constant This relatively long plateau corresponds with the very short one seen in the hyperventilation experiment with nitrous oxide The difference in height of the plateau for the carbon monoxide and nitrous oxide curves can be explained by the hyperventilation and the different diffusion constants for the two gases

In the blood phase, the concentration curves for carbon monoxide are not [illegible] images of the tension [illegible] reaches about [illegible] ion occur and cause a change in the horizontal plateau in the gas phase The curves for this rise in blood concentration in Fig 53 are those given by Forbes, Sargent and Roughton (1945), though in the figure they are expressed not as absolute values but as a percentage of the equilibrium value The latter, for the two concentrations of carbon monoxide shown (0 1 and 0 3 per cent), represented 62 and 86 per cent carboxyhaemoglobin in the blood respectively at time infinity, and was found by extrapolation Our results for the gas phase in some confirmatory experiments agree with those of Forbes and others, since after the inhalation of 0 3 per cent of carbon monoxide for about 10 minutes, we found the horizontal plateau was followed by an upward trend

In Fig 53 the curves for the gas phase of carbon monoxide after back-tension starts to rise are shown dashed because their form is not known They must reach 100 per cent at the same time as the equilibrium level in the blood occurs, though they are no longer mirror images of the blood concentration curves

Thus, we can summarize the form of the time-expirate concentration curve for carbon monoxide in the lungs over a series of breaths by referring to four phases (1) the phase of mixing from ambient to alveolar air deviating from the helium curve because of concurrent absorption, lasting about ten breaths,

and terminating in a sharp inflexion, (2) a phase, lasting about 10 minutes, when the rate of uptake of the gas is constant while there is negligible back-tension so that there is a horizontal plateau to the curve, (3) a phase of rising back tension, slowing of the rate of uptake and rising concentration in the expirate which lasts about ten times as long as the previous phase, (4) a second phase of equilibrium when no further uptake occurs, which can only safely be observed with very low concentrations of carbon monoxide in the inspired mixture

Our experiments have given us information about the first and second phases of carbon monoxide uptake It is the height of the plateau in the second phase which is measured by our carbon monoxide results and which we shall discuss in Section 3 (p 183)

2. Interpretation of Helium Results

A THE BASIS OF GAS REPLACEMENT EXPERIMENTS

Previous workers have used inert non soluble gases for the investigation of gas distribution within the lungs, either by analysing a single expiration following inhalation of a diluent gas or by serial analyses of either the process of 'uptake' or 'wash-out' in the lungs by the diluent gas using a closed- or an open-circuit apparatus We are concerned mainly with serial measurements of gas-replacement, since these are directly comparable with our own The essence of the method is to construct a curve relating time or number of breaths from the start of the experiment to the degree of gas replacement in the lungs, as measured by the change in concentration of the diluent gas in the expirate The interpretation of the results depends both on precisely what is measured (the type of curve) and exactly how the measurements are made (the apparatus and sampling method)

Type of Curve

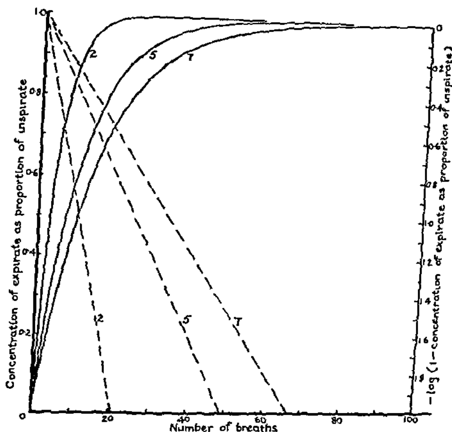
By using a non absorbable gas the intermittent process of breathing rather than the continuous one of gas absorption is measured, thus one of the fundamental parameters is the tidal volume We think the curves should be expressed with the number of breaths from the start of the experiment and not time as the abscissae, since the rate of breathing may vary considerably, especially between one subject and another On this point we agree with most other workers though Meneely and Kaltreider (1949) and Robertson, Siri and Jones (1950) have used time Often the difference in interpretation is immaterial, but sometimes approximations may not be justified when a continuous mathematical conception is applied to the tidal process Even more important is what the ordinates express, for two distinct types of curve are possible, increment or accumulation curves, which have not been explicitly distinguished by other workers (see p 69)

Apparatus

Open-circuit The known variables will affect the number of breaths for replacement in the manner expressed by the equation representing the perfect-mixing model

$$C_{T_r} = 1 - \left(\frac{F}{F+T}\right)^r \quad \text{or} \quad 1 - q^r$$

Small changes in the value of the alveolar expansion ratio, q, may produce large changes in the number of breaths required for gas replacement in the lungs, for the number increases rapidly as q approaches 1 In Fig 54 theoretical



... curves for three values

replacement curves are plotted assuming a constant tidal volume of 500 ml and functional residual capacities of 2, 5 and 7 litres, which represent common values in normal subjects, those with advanced pneumoconiosis and those with severe emphysema respectively The shape of the curves changes as q increases and the N_{90} becomes rapidly greater

Since the N_{90} is inversely related to log q (p 72) a graph of the relationship shows how critical the ratio q becomes after about 0 9, when small changes in its size cause a large increase in the number of breaths required for replacement of the gas in the lungs (Fig 55)

Closed circuit With this apparatus only an accumulation curve is analysed, for the changing composition of the inspirate would make the interpretation

of the increment curve very difficult, the accumulation curve is, however, directly comparable with that obtained or calculated for the open-circuit apparatus

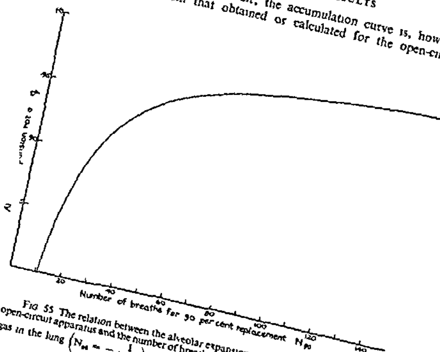


FIG 55 The relation between the alveolar expansion ratio (q) as measured on an open-circuit apparatus and the number of breaths required to replace 90 per cent of the gas in the lung $\left(N_{90} = -\dfrac{1}{\log q}\right)$ assuming perfect mixing.

As in the open-circuit, the known variables (tidal volume and functional residual capacity) determine the number of breaths required for gas replacement in the lungs apart from any inequality of mixing However, in the closed-circuit the volume of the machine (Vm) will also affect the rate of gas mixing and is therefore important If, for example, the volume happens to be the same as the functional residual capacity, the N_{90} for the closed-circuit would be about half that for the open-circuit and so on

$$\frac{N_{90}^{Tb} \text{ closed}}{N_{90}^{Tb} \text{ open}} = \frac{\log_e q}{\log_e Q} \qquad (14)$$

$$\simeq \frac{T/F}{T/F + T/Vm} \, ^{*}$$

$$\simeq Vm/F + Vm$$

$$= \tfrac{1}{2} \text{ when } Vm = F$$

The larger the volume of the closed-circuit machine the greater the number f breaths for a given degree of gas-replacement until in the limit, when the

* Just as $\log_e q$ is approximately $-T/F$ when T is small compared with F (see footnote on [151]) so $\log_e Q$ is, from a similar argument approximately $-(T/F + T/Vm)$ ... all compared with Vm.

volume is infinite, the Q of the closed circuit becomes identical with the q of the open circuit, and the number of breaths for a given degree of gas replacement in the lungs, as observed in the two pieces of apparatus, becomes the same (Appendix III)

Methods

As Bateman, Boothby and Helmholz (1949) have pointed out, either 'end point' or 'serial' sampling may be used End point sampling consists of the tedious process of stopping the experiment after a given number of breaths,

consists of obtaining a continuous record of the changing mixed expirate in the spirometer, or, if the increment curve is followed, of sampling any breath as it is expired Serial sampling is clearly the more convenient method since it

lungs during the inhalation of pure oxygen, can be followed Most American workers have used open circuit nitrogen wash out (Darling, Cournand and

nitrogen (Wolfe and Carlson, 1950) Cournand and others (1940) followed both the uptake and wash out of nitrogen on a closed circuit apparatus

The use of nitrogen, by whatever method, is complicated by its greater solubility in blood than that of the other two gases so that the results must be corrected for the entry or exit of nitrogen to or from the blood, during the replacement Measurements of intrapulmonary gas replacement by uptake of helium are more satisfactory because loss into the blood is thought to be negligible and correction unnecessary On the other hand, its use has been criticized because of its unusual physical properties although its viscosity is practically the same as that of nitrogen, its low density and resulting rapid diffusion might make its mode of replacement different from that of a 'physiological gas However, it is improbable that the differences between these two gases produce a large effect because our helium results agree within experimental error with the corrected nitrogen results of other workers (p 173) The corollary supports the contention that gas flow produced by breathing and not diffusion is the main mechanism of gas replacement and hence the number of breaths is a better parameter than time for the curves

B GAS-REPLACEMENT UNCORRECTED FOR KNOWN VARIABLES

time or number

'mixing time' on a closed-circuit apparatus and showed that it was prolonged in emphysema Boothby, Lundin and Helmholz (1948) effectively used exactly the same type of measurement when they noted the point at which a nitrogen wash-out curve, plotted on double logarithmic paper, showed a final bend and became linear This point was considered to be the completion of wash-out, the subsequent linear change only representing nitrogen elimination from the blood Meneely and Kaltreider compared their results with an alternative procedure, introduced by Cournand, Baldwin, Darling and Richards (1941), of measuring the degree of wash-out after a given time This last procedure, which has been commonly used, is called the 'pulmonary emptying rate', which is found by estimating the alveolar nitrogen after washing out the lungs with oxygen for a standard time on an open-circuit apparatus

These indices, however, take no account of change in the known variables, tidal volume and functional residual capacity, which were shown (Fig 54) to influence markedly the replacement time or breath number apart from any ventilatory inequality in the lungs

Apart from the limitation of their possible interpretation, any of the uncorrected indices of gas-replacement affords only an insensitive means of differentiating normal from abnormal subjects The longer the experiment proceeds the greater this differentiation, but, at the same time, the repeatability of the results decreases so that there is little gain in sensitivity

Fowler (1950) reports a coefficient of variation of about 50 per cent for the mean alveolar nitrogen values after different times of wash out in normal subjects His figures suggest a slight improvement in discrimination of normal from emphysematous subjects up to a 5 minute wash-out time, which is the longest time quoted Motley, Lang and Gordon (1949) give values for the alveolar nitrogen after 7 minutes oxygen wash-out which "show a progressive increase as the degree of emphysema increases, however, the individual variations are large" Some of their 'far-advanced' emphysema group have values in the middle of the normal range

Our closed-circuit results (Table IV, p 232) for the accumulation N_{90}, which corresponds with the index used by Meneely and Kaltreider, and also the open-circuit increment N'_{90} (Table X, p 238) and N'_{90} showed very poor differentiation between normal and abnormal subjects * Although the more complete the replacement the bigger the difference between the groups, the more difficult it becomes to identify the required point owing to the asymptotic nature of the replacement curve

In conclusion, it appears that tidal volume and functional residual capacity themselves show enough variation, either because of differences in the size of men or because of disease to make simple, direct indices of the rate or number of breaths for gas-replacement unsatisfactory and insensitive when they take no account of the known variables It so happens that subjects with much inequality tend often to have big lungs, we, therefore, agree with a comment by Bateman (1950b) "It can be predicted on the basis of lung volume measurement alone, that in persons with certain types of emphysema nitrogen clearance would be prolonged and measurement of the clearance curve would provide little

* The open-circuit actual N_{90} is no greater than the closed-circuit N_{90}, whereas theoretically it should have been (p 157) This is, we think, due to the relative insensitivity of the quicker responding open-circuit katharometer, which meant that the open-circuit curves were not taken to such complete replacement This only affects the direct comparison of the two kinds of apparatus and not the argument here

We conclude that the index is at present too dependent on technique to make results of different workers comparable *We think that technical defects in the closed-circuit apparatus do not account for the variation in the normals and the rather poor discrimination of the index* I_0, *since the same index on the open* [illegible]

We agree with Bates and Christie that *its interpretation* must be as a measure of the effect of the upper respiratory dead space *which prevents part of the* tidal volume reaching the lower parts of the lung *where mixing is taking* place, together with any inequality of ventilation in this *part, it is for this* reason that we have called the index 'overall'

Other Empirical Indices

The total ventilation for gas replacement Wolfe and Carlson (1950) described a "new index of ventilatory efficiency, the 'mixing index', which takes into account variations in minute volume and lung size' This index, the functional residual capacity divided by the total ventilation to reach equilibrium was based on the conception that the greater the ventilatory inequality in the lungs, the greater the total amount of gas required to replace that already occupying the functional residual capacity It is a measure of the overall ventilatory inequality like the index I_0 and can, in fact, be directly related to it Since, however, Wolfe and Carlson worked with a closed circuit apparatus the actual value of their index depends partly on the volume of their particular piece of apparatus (p 157) This volume is not given in their paper, but since the values they give for their index for three normal subjects are 21, 15 and 14 per cent (approximately one fifth of our normal values for I_0, Table IV, p 232), it suggests that the volume of their apparatus must have been about 6 litres, that is approximately twice the average functional residual capacity This can be deduced from the interrelation of their index to I_0 It was assumed that 'equilibration' was 99 9 per cent replacement Then

$$I_0 \text{ at } N_{99\ 9} = \log_{10} 0\ 001/N_{99\ 9} \log_{10} Q^*,$$

$$= -3\times 2\ 303/N_{99\ 9} \log_e Q,$$

$$\simeq 3\times 2\ 303/N_{99\ 9}\ (T/F+T/Vm)$$

$$\text{or when } Vm = 2F,\ I_0 \simeq 2\times 2\ 303\times F/(N_{99\ 9}\times T)$$

$$\simeq 5F/\text{total ventilation to equilibrium}$$

The relation of increment to accumulation curves This has been discussed on [illegible] gives a visual

p 71, and [illegible] make the index numerical would be time consuming and there are more sensitive and useful numerical indices which can be calculated from the data (see I_R and I_B below)

---

* $I_0 = \log_{10}$ (fraction unmixed) $/\log_{10} Q$ (see p 58)
$= -1/\log_{10} Q$ for 90% mixing
$= -2/\log_{10} Q$ for 99% mixing
$= -3/\log_{10} Q$ for 99 9% mixing etc

Analytical Indices

Post-dead-space Ventilatory Inequality

In the overall indices discussed above, the patient's performance is compared with a perfect-mixing system which does not take into account the effects of an upper respiratory dead-space In fact, a dead space is present, and theoretical equations show (Appendix III) that it alters the concentration of trace gas exhaled after a given number of breaths for a given tidal volume; the space is included in the functional residual capacity, but must be subtracted from the tidal volume, so that only the effective tidal volume enters the mixing chamber at each breath

One of the first analytical procedures is to determine the influence of the dead space on the overall indices If the dead space itself is altered in such conditions as emphysema it may be an important part of the inequality expressed by the indices, if not, and the functional lesion of such conditions is mainly poor distribution of air in the remainder of the lung, the inclusion of the dead-space effect, by the comparison of the subject's performance with a model without dead space, will merely lead to insensitivity of the indices There is a large volume of literature on dead-space, but its precise definition in man has only recently been made clear, so that we shall summarize this before proceeding with the interpretation of the post-dead-space indices

Upper respiratory dead space The simplest concept of dead space used to be that of the anatomical airway being completely refilled at the end of one inspiration by a quantity of gas, which was then exhaled unchanged at the beginning of the next expiration and followed by alveolar gas of a different but constant composition This concept is nearly true for normal subjects, and the volume of the upper respiratory space, calculated from the Bohr equation, corresponds reasonably well with the volume of the airways measured anatomically at post mortem

However, in many abnormal subjects, especially those with emphysema in whom there was no marked change in volume of the trachea or increase in size of the bronchi at autopsy the dead space calculated from the Bohr equation does not agree with the anatomical dead-space Recent work has shown that this is because the alveolar gas varies in composition, so that the calculated value depends on the time during the later phase of expiration when the alveolar sample is taken The apparent enlargement of the dead-space when it is calculated in this way could therefore be explained as ventilatory inequality in different areas of the lung causing greater heterogeneity of the alveolar gas than in normal subjects

It is now recognized that there are three distinct values (1) the 'anatomical' dead space which is the volume of the upper respiratory passages measured after death or calculated by fluoroscopy in life, (2) the 'calculated' dead-space obtained from the Bohr equation (3) the 'kinetic' dead space described by Lilly (1950) as the total volume of gas required to wash out the upper respiratory passages after which alveolar gas is expired

Fowler (1948 1949) made a rapid, continuous record of the nitrogen oncentration and the volume of gas expired after one inspiration of oxygen, nd showed that the alveolar 'plateau' is approximately flat in normal subjects ig 17, p 78). The calculated dead space is therefore about the same hatever point on the volume-concentration curve (after the sharp S bend) is ected for the alveolar sample in the Bohr equation, the use of an agreed

point early in the alveolar plateau largely eliminates any effect of uneven alveolar-nitrogen content In abnormal subjects, it is not easy to select the *initial point because the alveolar plateau is so steep, but Fowler took a* ventilatory criterion for the identification of alveolar gas (for the full meaning of which his paper must be consulted), and *in this way showed that the kinetic* dead space was not enlarged in abnormal subjects compared with normal ones The average value of the kinetic volume in normal subjects was 325 ml (S D 65 ml) during quiet breathing, but was increased to 526 ml (S D 118 ml) on maximum ventilation

Thus, the *meaning of upper respiratory* dead space becomes simplified (1) The upper respiratory passages have a certain volume which is not much changed in emphysema, gasometric determination of this volume (calculated or physiological dead space) is only practicable when the alveolar gas concentration can be defined This is simple in normal subjects, possible in some abnormal *subjects by refined methods*, but impossible in grossly emphysematous cases (2) The volume of gas required to replace completely that already in the upper respiratory passages (kinetic dead space volume) is greater than the volume of the passages themselves The kinetic volume changes with the depth of respiration but varies little in disease, even though the alveolar gas-concentration may be altered so that the 'calculated volume shows an apparent increase

The residual index I_R. It is evident that if an alveolar sample is taken at a constant time after the start of expiration, provided the kinetic dead space has been expelled, then variations in this sample can give a measure of ventilatory inequality in the post dead space parts of the lungs, or, to quote Rauwerda's terms from his comprehensive review of ventilatory inequality (Rauwerda 1946), *it will reflect the 'regional inequality' of ventilation in the lungs apart* from any 'stratified inhomogeneity' due to dead space Such a sample is the basis of our index I_R

Our open circuit apparatus automatically took a small expirate sample (about 12 ml) at 1 3 seconds after expiration started and pneumotachogram studies *showed that the greater part of the tidal volume* (approximately 70 per cent, depending on the size of the tidal volume itself) had been exhaled by then Thus the subject's kinetic dead space of about 300 ml had been cleared, and the summation of the acceptance ordinates above the recorded increment curve gave a value for the functional residual capacity in terms of an effective tidal volume *The size of this effective* tidal volume is partly a function of the apparatus However, it is interesting to note its approximate size in our results, and some idea of this was obtained by relating the tidal volumes to the corresponding effective [illegible] *onal residual* [illegible] nates of the [illegible] 7 where the [illegible] tidal volume [illegible] ter of points about the regression line although, consider [illegible] *d from two* pieces of apparatus between which the subject's tidal volume undoubtedly varied, the results agree well with what would be expected They are of interest for two reasons first, although they are a very crude estimate of kinetic dead space, they agree with the work of Fowler in showing no marked difference between normal and abnormal subjects, secondly, the kinetic dead space varies with the tidal volume, a fact which is now generally accepted (Moncrieff, 1933,

(cited b [illegible]
conside
below
coniosis and to be especially marked in the cases of non industrial emphysema (Figs 43 and 44, pp 120, 121)

The nature of *this residual inequality* measured *by* the index I_R can be discerned to some extent by a mathematical analysis of the form of the replacement curves This will now be considered *in relation to similar work by other* observers

The Nature of the Ventilatory Inequality

This discussion is mainly confined to the open-circuit replacement data which are simpler to analyse and less influenced by instrumental error than the closed For analysis, the acceptance data from the increment curve are *plotted on a logarithmic scale against breath number* on a linear scale (*Fig 58*), the graph is thus a logarithmic plot of the summation of the ordinates above the increment curve and so, because of the nature of the *sampling represents* the building up or replacement of the functional residual capacity in units of effective tidal volumes

[illegible] ented the process

(*p 72*) *In fact, even in normal subjects to a slight extent as shown in Fig 58*, and in abnormal men to a much greater extent, it was found that the graph was curvilinear initially, becoming straight only after about 10 or 15 breaths

[illegible] one component

The experimental curve can be analysed into these two components [illegible] *simplest mathematical model which fits such an analysis* (*Appendix III, Section* 4, p 257) is one in which the whole functional residual capacity is regarded as *consisting* of two parts behaving like chambers in parallel (F_A and F_B) a proportion of the effective tidal volume going to each (T_A and T_B respectively) Perfect mixing is deemed to occur in each chamber but the expansion ratios of the two components differ so that replacement is completed in the one say F_B before it is in the other, or, in other words the ratio of T_B to F_B is greater than that of T_A to F_A

It must be understood that other mathematical models besides this form of post dead space parallel inhomogeneity, also fit the results and can represent a

[illegible]

7

But the simple two chamber in parallel model [illegible] it purpose, since we are now only concerned *with the point that the experimental* data (both open and closed) demand more than one exponential process taking part *in post dead space mixing*, so that one portion of the lung appears to be hyperventilated compared with the rest and gas replacement is completed there first.

It can be shown (Appendix III, p 257) on the basis of the simple biphasic model, how numerical values can be given to the postulated volumes F_A and

F_B together with their respective tidal volumes In Fig 58 the linear portion of the experimental curve (heavy line) represents the more slowly replaced volume F_A acting alone, so that the slope of this line is the logarithm of the

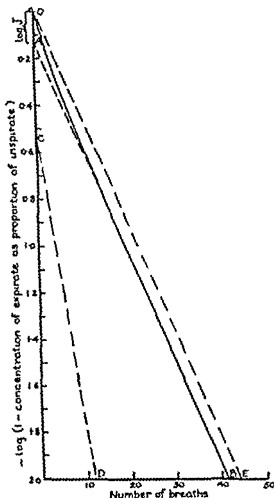


FIG. 58 Semi-logarithmic plotting of the increment curve (acceptance ordinates 1 – y) related to the number of breaths. Mean values of normal subjects aged 25

expansion ratio of F_A that is $\log q_A$ The slope of the line CD obtained from the differences between the curve and the extrapolation of AB represents $\log q_B$ The distance $\log J$ from the origin to the cutting point of the extrapolation of AB gives the proportion of the effective tidal volume going to F_A

and OE, which is the index I_a represents the degree of departure from a s[illegible]

exponential system, on account of the presence of the small, rapidly replaced portion F_B

Whatever the true model for intrapulmonary gas-mixing (and, on a serial mixing model, p 260, the hyperventilated portion F_B might even be an extension of kinetic dead-space), we believe that it is useful practically to analyse the crude data, first by eliminating the effects of the kinetic dead-space, either automatically in the apparatus or by computation, and secondly by expressing the degree of the remaining inequality By this method an index more discriminating for the effects of ventilatory inequality is obtained Both I_R and I_B are this type of analytical index and can be related mathematically

The relation of the indices I_R and I_B.

$$I_R = -100/(N_{90} \log_{10} q') \qquad \text{(equation 7, p 73)}$$

and
$$I_B = \log_{10} J/\log_{10} q_A,$$

but
$$q' = \frac{F}{F+Te} \text{ and } q_A = \frac{F_A}{F_A+T_A} \text{ and } T_A = J\ Te$$

Now the volume of the rapidly replaced portion of the lungs was found to be small in all cases (cf Tables XI and VIII), so that if F_A is a large fraction of F and always much greater than Te,

$$q_A \simeq \frac{F}{F+J\ Te} \simeq (q')^J$$

$$\therefore \log_{10} q_A \simeq J \log_{10} q'$$

and
$$I_B \simeq \log_{10} J/J \log_{10} q'$$

and
$$I_R/I_B \simeq -J/N_{90} \log_{10} J.$$

The inequality in emphysema The small group of five men with advanced emphysema provides a comparison with the normal group in revealing the ... of the functional change which takes place

is seen in the advanced emphysema group ... age and with pneumoconiosis; thus, the changes are on the whole progressive down the columns

TABLE 23

Ventilatory inequality of the lung expressed in terms of the components of a two-phase perfect mixing system group means for 10 normal subjects, 8 men with category D pneumoconiosis and 5 men with non industrial emphysema

Group	Tidal volume T (ml)	Effective tidal volume Te (ml)	T_A (ml)	$J = T_A/Te$	Expansion ratio q_A	Index $I_B = \log J / \log q_A$	Functional residual capacity F (l.)	F_A (l.)	F_B (l.)	F_B/F (%)
N_{ss}	754	455	324	0 731	0 902	3 2	3 31	2·92	0·39	12
N_{sa}	894	484	315	0·694	0·909	4 3	3 92	3 32	0·60	15
D_{ss}	593	424	198	0 478	0 936	11 8	3 58	2 91	0 67	19
Emphysema	662	589	258	0 450	0·951	16 8	6 11	5 27	0 84	14

It is seen that the value of J which represents the proportion of the effective tidal volume going to the major component (F_A) decreases with abnormality. At the same time the absolute volume of the *hyperventilated* portions of the lungs is increasing though its size relative to the whole lung volume remains small and about constant Comparison of the carbon monoxide and helium data (p 193) suggests that *the* gas uptake within the hyperventilated portion is actually relatively reduced in a lung where the whole gas transfer is deficient and *no* longer fits the helium phases thus in emphysematous conditions less of the effective part of the *inspirate* is distributed to the main gas absorbing volume

It will also be seen that there is a steady increase in the expansion ratio q_A (reflecting the decrease in slope of the linear part of the graph) The change in this ratio may appear small but it is important since the ratio is approaching unity which means a large increase in the number of breaths required to replace the gas in part of the lungs (Fig 55 p 157) This increase in the ratio q_A which is $F_A/F_A + T_A$ mainly reflects the decrease in T_A though in the emphysema group but not in the pneumoconiosis group D_{ss} F_A itself is increased in spite of the increase in F_B There is in other words an increase in the whole functional residual capacity

The above findings may be summarized by saying that the functional emphysematous lesion is a maldistribution of the effective tidal volume less of it going to the main portion of the lungs When the whole of the functional residual capacity is *increased* the effects of the maldistribution are enhanced and the number of breaths required for gas replacement becomes all the greater

The index I_B is sensitive because both factors (the increase in log J consequent in the reduction of T_A and the increase in q_A) enter the index in an opposite sense since I_B log J log q_A The index appears reasonably specific for although a relative reduction in T_A may occur in hyperventilation in truly normal subjects if the q_A ratio is not also abnormal the index I_B remains within normal limits In other words the index is relatively independent of hyperventilation though we have not made any separate experimental studies of the effect of large variations in rate and depth of breathing (keeping the total ventilation constant) on the inequality of ventilation in normal subjects measured in this way

It is interesting that the emphysematous lesion appears to be an exaggeration of a change which takes place with an increase in age in normal subjects

Results of Other Workers

Open circuit Darling, Cournand, Richards and Domanski (1944) made some of the first serial wash out experiments on intrapulmonary gas mixing They used the technique of end point sampling developed from their open-circuit method of estimating residual capacity (Darling Cournand and Richards, 1940) Having calculated an *appropriate theoretical curve which would express the nitrogen* remaining in the lungs after different numbers of breaths of oxygen they compared these concentrations to those found on experiment both by direct alveolar sampling and by deduction from the samples of the nitrogen accumulated in the collecting spirometer In most normal subjects these two experimental nitrogen results agreed with the predicted values, but in some (mostly elderly) the nitrogen remaining in the lungs was greater than that expected *so that the alveolar value differed from that given by the accumulation curve* This suggested regional inequality to the authors and it was much more marked in their emphysematous subjects Thus their finding that 'imperfect intrapulmonary mixture in some normal subjects is probable' agrees with ours However, their method is open to the serious objection, which they acknowledge, that it required the assumption of a value for the respiratory dead space obtained from Bohr's equation although the alveolar sample value itself was *one of the indications of imperfect mixing*

Bateman (1946) argued that imperfect mixing can conveniently be expressed as apparent enlargement of dead space. He extended Cournand's open circuit technique by introducing a form of serial sampling (Bateman Boothby and Helmholz 1949) to save the tedious replicate experiments of the end point [illegible] the intrapulmonary mixing of 20 normal [illegible] ection for nitrogen [illegible] *should be directly* [illegible] different [illegible]

In making the comparison it must be realized that, although the curves look superficially the same Bateman's are accumulation and ours increment curves Therefore, in Fig 59 we have replotted the average result for our subjects [illegible] the accumulation [illegible] with the correspond[illegible] [illegible] normal subjects agrees both in slope ($q_A \simeq 0.9$) and in cutting point with Bateman's figures the average slope of his log plots for his normal subjects being 0.91 (S.D. $= 0.04$)

Bateman however, interprets his results as showing that the single-chamber model is valid for normal persons *while recognising that further study might establish the existence in some instances of more than one exponential clearance process* We do not find that the single-chamber interpretation fits normal subjects first, while sympathizing with his desire to include only experiments in which the tidal volume was regular, we think the inclusion of only 13 out of 47 experiments may have meant that some *curvilinear results* were mistakenly rejected as incorrect especially in elderly subjects of which few are included *in his series secondly* the use of the accumulation curve means that the cutting point of the log plot is nearer the origin than it is in

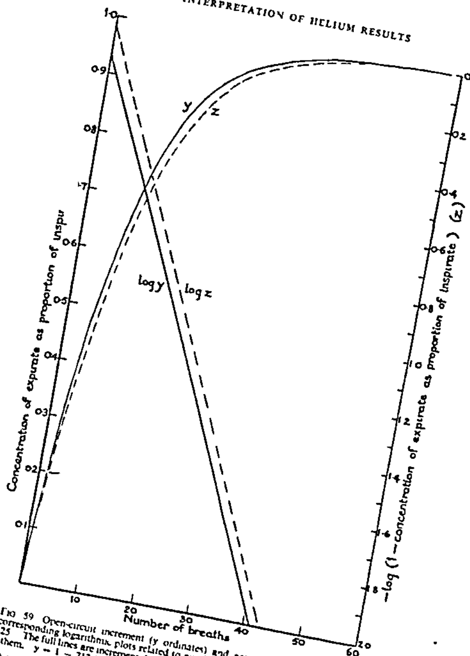


FIG 59 Open-circuit increment (y ordinates) and accumulation (z ordinates) curves and corresponding logarithmic plots related to number of breaths. Mean of normal subjects, aged 25. The full lines are increment data and the dotted ones accumulation curves calculated from them. $y = 1 - 712\,(q)^n - 288(746)^n$ $z = 1 - 884(q)^n - 116(756)^n$

Cutting points T_A = 884 and T_A T_e = 712, for log y and log z respectively, apply to the anti-log of the right hand scale

the corresponding acceptance curve (Fig 59), and this *may lead to the inter*pretation of a single linear phase right up to the origin

The cutting point *of the log-accumulation* curve represents the ratio F_A/F rather than the ratio T_A/Te of the increment curve It is shown (Appendix III, *equation 106a, p 258)* that the equation for the perfect-mixing biphasic model is, for increment data,

$$1-CE_r = (T_A q_A{}^r + T_B q_B{}^r)/Te$$

where T_A/Te is the intercept for the linear part of the semi logarithmic plot But the accumulation data *represent*

$$\sum_0^r (1-CE_r) \Big/ \sum_0^\infty (1-CE_r) = 1-z_r$$

or

$$1-z_r = 1-\{(F_A+T_A)q_A{}^r+(F_B+T_B)q_B{}^r\}/(F+Te)$$

[illegible] plot therefore $(F_A+T_A)/(F+Te)$ in this [illegible]

young normal subjects can be seen from the equations in Fig 59

Other American workers have thought that normal subjects do not necessarily conform to a single perfect-mixing system, Jones (1950) concluded from nitrogen wash-out experiments that the usual normal subject "has two major rates of ventilation of the lung gas field", though other subjects, not included in the group reported, were found to have only one discernible mixing rate of 0 45 minutes half-time In a later paper more detailed results are given (Robertson, Siri and Jones, 1950) together with a *mathematical* analysis of them, their analysis produces some illuminating ideas on a theoretical model of *the process of mixing and we discuss it again later (p 181) Here we are only* concerned with their experimental data in relation to our own

The method used by Robertson and others was to pass each expirate *through* a 400 ml baffle chamber on the way to the collecting spirometer, so that a very small sample of gas bled from this baffle reflected the expired concentration of nitrogen as a continuous change with time The gas was analysed by a mass spectrometer from the start of the wash-out with oxygen until 10 minutes had elapsed The results were plotted on semilogarithmic paper so that analysis could be easily performed in the usual way Owing to the nature of the method *the changes in gas concentration were expressed* relative to time rather than to number of breaths The results are expressed as a 'turnover rate' for each *exponential component together with the proportion* of the functional residual capacity with which it is associated Besides this analytical result a single 'efficiency index' is given in which the turnover rate of *the homogeneous* [illegible] mental data is compared with an equivalent perfect- [illegible]

of the functional residual capacity with which they [illegible]

compare their normal data with our own, some of the curves were reconstructed from their tables and plotted as semilogarithmic increment curves *

[illegible] the fraction of the [illegible]

linearity and a greater apparent enlargement of dead space. However we prefer a method of presentation in which uneven ventilation is distinguished from the effects of the existence of an upper respiratory dead space

An alternative though tedious method of analysis of our closed circuit curves was made on the assumption that the whole log plot was really curvi linear An equation to represent this has the form (see Appendix III)

$$Cm_r = 1 - Q^{ar^c}$$

where a = the proportion of the tidal volume which is effective (Te/T) and c is a number to which we have not been able to attach a physical meaning but which is an index of the inequality since it measures how much the curve deviates from that predicted for a perfect mixing system of the observed functional residual capacity and tidal volume, after allowance has been made for the upper respiratory dead space

It can be shown that $c = \log N_{90}^{Th}/\log N_{90}$ and it is thus a log ratio equivalent to the indices $I_O = 100N_{90}^{Th}/N_{90}$ when the N_{90}^{Th} is derived from Q for the closed circuit and $I_R = 100N_{90}^{Th}/N_{90}$ when N_{90}^{Th} is derived from q for the open circuit apparatus

This form of analysis was not done in all subjects but a representative sample showed there to be good relation between closed and open-circuit results This confirmed the hypothesis that it was allowance for the presence of the dead space rather than the intrinsic difference between open and closed circuit apparatus which made the indices I_R and I_B more useful than I_O It shows the significance of Birath s use of the apparent enlargement of dead space and emphasizes the difficulty of using closed-circuit data for mixing results compared with the simplicity of the open-circuit

Briscoe Becklake and Rose (1951) published some closed-circuit helium experiments on intrapulmonary gas mixing after our experiments had been completed They plotted an accumulation curve obtained by end point sampling against the number of breaths on an algebraic scale This procedure converted the curves to a sigmoid shape and they were compared on the same axes with the corresponding sigmoid curves for a single chamber perfect mix ng system These authors have since altered the sampling procedure and pr[illegible]

[illegible] pparatus

to [illegible] simpler

and more useful presentation of the results [illegible] es were plotted semilogarithmically but their analysis was only superficially similar to the analysis of open circuit results by other workers By his analysis Briscoe found two main ventilatory phases in the lung—an initial one corresponding to a major portion and a minor slower mixing phase occurring late in gas replacement Using his method on our closed-circuit results we too find a [illegible] phase but only in occasional subjects usually those with [illegible] nal th rd [illegible] ve [illegible] nt [illegible] er

replacement the curves were linear on [illegible] this range there was one exponential component and that before 70 per cent mixing (that is up to about 9 breaths) the results were compatible with one other hyperventilated component but our data for this part of the process were not precise enough to warrant any further analysis It is possible that

linearity and a greater apparent enlargement of dead space However we prefer a method of presentation in which uneven ventilation is distinguished from the effects of the existence of an upper respiratory dead space

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$$Cm_r = I - Q^{arc}$$

where a = the proportion of the tidal volume which is effective (Te/T) and c is a number to which we have not been able to attach a physical meaning but which is an index of the inequality since it measures how much the curve deviates from that predicted for a perfect mixing system of the observed functional residual capacity and tidal volume, after allowance has been made for the upper respiratory dead space

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late hypoventilation ph

advanced emphysema

phase given by Fowler

could certainly say was that between the stages of about 70 and 99 per cent replacement the curves were linear on the semilogarithmic plot so that over this range there was one exponential component and that before 70 per cent mixing (that is up to about 9 breaths) the results were compatible with one other hyperventilated component but our data for this part of the process were not precise enough to warrant any further analysis It is possible that

linearity and a greater apparent enlargement of dead space. However, we prefer a method of presentation in which uneven ventilation is distinguished from the effects of the existence of an upper respiratory dead space

An alternative though tedious method of analysis of our closed circuit curves was made on the assumption that the whole log plot was really curvi linear An equation to represent this has the form (see Appendix III)

$$Cm_r = 1 - Q^{arc}$$

where a = the proportion of the tidal volume which is effective (Te/T), and c is a number to which we have not been able to attach a physical meaning, but which is an index of the inequality *since it measures how much the curve deviates from that predicted for a perfect mixing system of the observed functional residual capacity* and tidal volume, after allowance has been made for the

ratio equivalent
to
for the closed
cir
for the open
circuit apparatus

This form of analysis was not done in all subjects but a representative sample showed there to be good relation between closed- and open circuit results *This confirmed the hypothesis that it was allowance for the presence of the* dead space rather than the intrinsic difference between open and closed circuit apparatus which made the indices I_R and I_B more useful than I_0 It shows the significance of Birath's use of the apparent enlargement of dead space and emphasizes the difficulty of using closed circuit data for mixing *results compared with the simplicity of the open circuit*

Briscoe Becklake and Rose (1951) published some closed-circuit helium experiments on intrapulmonary gas mixing after our experiments had been completed They plotted an accumulation curve, obtained by end point sampling against the number of breaths on an algebraic scale This procedure *converted the curves to a sigmoid shape, and they were compared, on the* same axes, with the corresponding sigmoid curves for a single-chamber perfect mixing system These authors have since altered the sampling procedure and presentation of their

In a subsequent pa ... pparatus
to give serial samplin ... simpler
and more useful presentation of the results The accumulation curves were plotted semilogarithmically but their analysis was only *superficially similar to* the analysis of open-circuit results by other workers By his analysis Briscoe found two main ventilatory phases in the lung—an initial one corresponding *to a major portion* and a minor slower mixing phase occurring late in gas replacement Using his method on our closed-circuit results we too find a late hypoventilation phase but only *in occasional subjects, usually those* with advanced emphysema This presumably corresponds with the occasional third phase given by Fowler and others (1952) In our open-circuit results, *all we could certainly say* was that, between the stages of about 70 and 99 per cent replacement, the curves were linear on the semilogarithmic plot, so that over this range there was one *exponential component, and that* before 70 per cent mixing (that is, up to about 9 breaths) the results were compatible with one other hyperventilated component, but our data for this part of the process were not precise enough to warrant any further analysis It is possible that

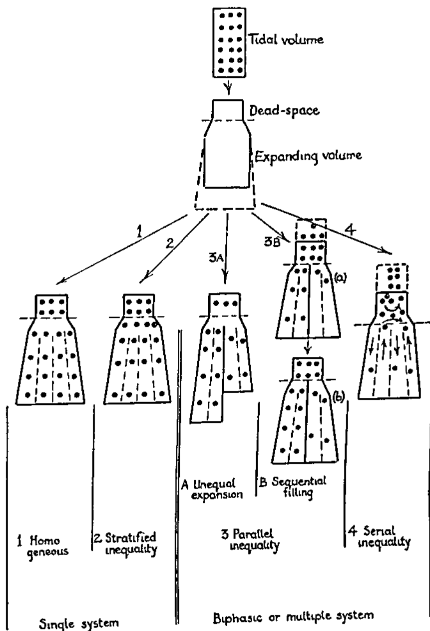


FIG 63 Diagram of concepts of gas replacement in the lung

eliminated Thus regional differences are demanded by such experiments as well as by serial measurements

Regional or 'parallel' inequality (scheme 3) would accord both with single-breath and serial experiments It might arise from either of two mechanisms unequal expansion in different portions of the lung so that the percentage
the latter does
that the dead-
those portions
which expand first" Clearly any simple model of parallel inequality assumes groups of tube systems to behave similarly giving rise to a biphasic system (as in the diagram) or a multiple system accordingly Equations describing the biphasic system are given in Appendix III (p 257)

Robertson, Siri and Jones (1950) were the first to point out that a 'series inequality' can also give rise to a biphasic or multiple system and can accord with the experimental results Such a system is indistinguishable, when observed by serial measurements of the expirate concentration, from the multiple exponential system which would arise from 'parallel inequality' Owing to their experimental technique, in which one expirate is mixed with another and the whole process of pulmonary wash-out is observed as a continuous change with time, they derive their models in terms of continuous change In Appendix III we have given an alternative analysis in which one tidal volume is the unit of change, and their concept is still valid This process is shown in Fig 63, scheme 4, where the inspired gas passes through a proximal (serial) mixing space, and from thence into a distal (alveolar) mixing chamber Due to turbulence in the proximal space, each element of gas mixture entering it mixes intimately with the contents of the space, before a representative part passes through to the distal chamber The fraction of inspired trace gas that can pass through such a serial mixing chamber into a distal chamber can be calculated for any postulated initial concentrations in these chambers (see Appendix III) Thus the concentration of gas in either chamber after a given number of breath cycles can be calculated

This cycle of operations, taking place at any breath, and an equation describing this sequence, can be deduced (equation 161, p 262) Two exponential processes result, though the constants for these processes cannot be deduced from the graphs We therefore agree with Robertson, Siri and Jones that serial inequality may give rise to a biphasic process, and any example of a serial mixing space, analysed as if it were in parallel, gives a value for the quickly mixing space in parallel similar in magnitude to the proximal serial space Our results are compatible with either parallel inequality or serial mixing

The assumption of serial mixing has many attractions gas entering the lung tube system must pass through and mix with gas in the proximal spaces

space increases with deeper inspiration as other workers have found The serial mixing equation which expresses the concentration of new gas leaving

the proximal space S, that is the *effective tidal volume after serial mixing has* taken place, is of the form $Te = 1 - e^{-T/S}$ In the simplest case, when $T = 2S$, then the effective tidal volume is 0 57 and when $T = 3S$, it is 0 68

It is probable that the complex arrangement in the human lung gives rise both to parallel and to serial inequality of ventilation If the evidence from the combined results of *open- and closed-circuit apparatus, together with that* from other workers, is all to be explained, a reasonable mechanism would seem to be one of serial replacement giving rise to the exponential components 1 and 2 (F_A and F_B) and parallel inequality to the third component called by Briscoe the poorly ventilated space, though component F_A may also be partly in parallel *On this assumption two lesions may proceed together in any* emphysematous lung an enlargement of F_B with associated maldistribution of the tidal volume and the development of the very slow mixing phase, particularly in those cases with large bullae The index I_B only directly measures the first change Lastly, we think there is little doubt about the advantage in *using mixing indices which allow for a constant, relatively large kinetic dead* space (as defined by Fowler), but, in so far as serial inequality is present, we suspect that the hypoventilated phase (F_B) may still represent an increase of kinetic (but not anatomical dead space) produced by change in the degree of turbulence in the bronchi or bronchioles

E CONCLUSIONS

There are two ways of investigating the effectiveness with which any tidal volume is distributed in the lung and so replaces the gas already there (1) by an analysis of the volume concentration changes in a single expirate, or (2) by following the clearance curves for the lung over a series of breaths In either method a foreign diluent gas is used in the inspirate It seems that single-breath experiments give the best estimates of the size of the upper respiratory dead space and hence of the effective tidal volume, serial replacement experiments [illegible] of gas in the

[illegible]

tion of the results for gas exchange *with the blood, and in this respect* [illegible] is preferable to the measurement of the clearance of the nitrogen in the lung by oxygen inhalation Since helium and corrected nitrogen results agree well there seems no 'physiological disadvantage in using the former gas, the choice depending partly on which is most easily analysed [illegible] or an open

[illegible]

circuit for clearance experiments first, the results are more co[illegible] to the changing concentration of the inspirate, secondly, the volume of the machine itself is a factor in their interpretation, and thirdly, lag in recording is less easily overcome owing to the time of mixing in the machine An arrangement which might prove satisfactory for clinical purposes would be to use helium in a closed circuit apparatus *for estimating the functional residual* capacity, then to wash out the lungs with oxygen and record the helium coming out in an open circuit apparatus using the same gas analyser The curve obtained as the result of clearance experiments may either express the change in concentration of gas breath by breath (increment curve) *or the summated change*

as the gas accumulates (accumulation curve), depending on the sampling method used In either curve, the results can represent the concentration of the gas rejected from the lung, or its complement, the gas 'accepted Only in a single exponential system, which implies even distribution and mixing of the tidal volume with the whole functional residual capacity at each breath ('perfect mixing'), are the increment and accumulation curves identical

The main practical difficulty in serial clearance experiments is in the expression of the results which are implicit in the particular clearance curve obtained Two principal methods have been used to define the ventilatory inequality, the first simply expresses the departure of the curve from the corresponding perfect mixing curve for the same tidal volume and functional residual capacity as that of the subject, the second is an analysis of the exponential components of the clearance curve and an expression of the different proportions of the functional residual capacity associated with them

In the first method, which is less informative but useful practically, different indices have been proposed by various authors which are actually interconvertible If allowance is made for the upper respiratory dead-space and the effective tidal volume used, the sensitivity and consequently the usefulness of the index is greatly enhanced, we have called such an index I_R

In the second method, which is preferred, the clearance curve is analysed into its components from a semilogarithmic plot of the data Our results in this method show that even in young normal subjects there is a biphasic clearance process a small part of the lung is ventilated more rapidly than the remainder and rapidly brought into equilibrium with the inspirate In old age, this biphasic clearance is more marked, but even then is slight compared to that in our cases of advanced emphysema The functional lesion in emphysema appears to be a maldistribution of the effective tidal volume giving rise to less even ventilation There is evidence that in advanced emphysema a third, very slow clearance process appears, though this accounts for only a small part of the whole gaseous replacement process These results are in complete agreement with those of most other recent workers and an explanation is given for most of the apparent discrepancies A single numerical index (I_B) is suggested as a practical index of the degree of biphasic clearance This index can be related to the index I_R

It is difficult as yet to determine the significance of the changes observed [illegible]

gas uptake Although clearance experiments are of great interest in the elucidation of functional pathology in the lung, their relative complexity still limits their clinical usefulness On the other hand, they may reflect changes in the lung not measured by other tests

3 Interpretation of Carbon Monoxide Results

As one index of lung function we measured the proportion of carbon monoxide removed from the inspirate during the second of the four phases of uptake which can be observed when this gas is inhaled This phase, described in

Section I (p 154), is the phase of negligible back tension in the blood, when the rate of uptake is constant (first equilibrium concentration) *Its level is a* function of the diffusion constant of the lung membrane (Kco) when all other variables were controlled, but in order to *interpret the meaning of the results* we must now examine what factors did influence this rate of uptake in the circumstances in which *we measured it*

We shall distinguish between the use of an 'average post dead space sample of the *kind taken automatically on every fourth* expiration with the open circuit apparatus (Part II, p 66), and an 'average expirate sample' representing *the mean* concentration of the whole of an expirate

A FACTORS INFLUENCING THE UPTAKE OF CARBON MONOXIDE

The factors which affect the rate of uptake of carbon monoxide in normal subjects have been studied by many observers These studies were reviewed by Forbes, Sargent and Roughton (1945), who showed by their own experiments, subsequently confirmed by Pace, Consolazio, White and Behnke (1946)

carboxyhaemoglobin *level* and *in the blood volume However, since in our test* we are merely concerned with the disappearance of the gas from the inspired *mixture, we can neglect the factors which only affect the rise in blood con* centration, provided we can show that no effective back tension occurred *which would alter the rate of removal of the gas from the lungs*

As the result of the work of Forbes and others, it is generally agreed that the rate of removal of carbon monoxide
factors (1) the concentration of gas in
exposure to the gas, (3) the ventilation
on the degree of activity, (4) the baror
centration in the inspired mixture, and (6) other variations dependent on the individual

Of these six factors, the gas concentrations in the inspired mixture remained constant, any small variations between one gas cylinder and another were compensated for by adjusting the sensitivity of the analyser to give *full de* flexion with the mixture and expressing the expirate concentration proportionately (p 67)

Because our results were expressed as the proportion of gas removed from the inspired mixture rather than as the absolute uptake, *they should theoretically* have been independent of variations in barometric pressure and, within limits, of the subject's ventilation The last statement is *essentially true because the* proportion of gas removed is expressed by the fraction

$$100(C_I\,T\,f - C_E\,T\,f)/C_I\,T\,f$$

However, the ventilation may, in practice, *affect uptake when alterations in* the respiratory quotient and breathing rate are large Thus, provided we establish that the time of exposure was *short enough to keep the blood CO* concentration at levels where no significant back tension occurred and that the variations in the ventilation between the *different subjects did not actually* affect our measurements, we may expect the changes observed to be due to the sixth factor, individual variations in the lung itself

Exposure Time

The test took between about three and seven minutes, depending on the time for complete helium replacement (because the gases were used con-

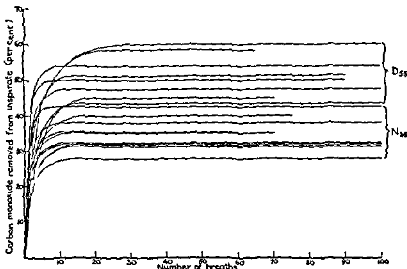


Fig 64 Increment curves showing the percentage of the inspired carbon monoxide rejected at each breath by individual subjects in the groups N_{35} and D_{55} The curves for all the intermediate groups were of the same general character

currently) From the results of Forbes and others this exposure time would

experiments until the blood carboxyhaemoglobin was between 20 and 30 per cent In practice, concentration of gas in the expirate did remain essentially constant during the time of our experiments, once the initial mixing-phase was complete This is shown in Fig 64

Ventilation

In Fig 65 the proportion of the carbon monoxide retained by each of the subjects in our experiment is plotted as a scatter diagram against their ventilation *There is no apparent relationship over the rather small range of ventilation observed*

Thus, since neither exposure time nor ventilation affected the results we may assume that the test measures changes in the lung itself

The Effects of Dead space

Forbes and others concluded, from a special pair of experiments carried out at rest on their slowest and fastest absorbers of carbon monoxide, that the individual variations, not explicable by changes of the five other factors, could only be due to variations either *in the ratio of tidal volume to dead-space or in the actual diffusion constant of the lung*, or both Since during the main

experiment we used an average post dead space sample, the effect of the upper respiratory dead space should have been removed

If an average expirate sample had been used, the tidal volume would have had some effect as observed by Forbes and others and Bates (1952)

The advantage of using an average post dead space sample instead of an average expirate sample is illustrated by an experiment in which four estimations were made of the carbon monoxide uptake of a normal subject trained in the use of our apparatus In two of the estimations he breathed with his usual tidal volume (about 800 ml) In the other two he about doubled his tidal volume but halved his respiratory rate, so keeping the ventilation practically constant In each case both types of sample were recorded The results are given in Table 25 where the independence of the average post dead space samples on the tidal volume is contrasted with the dependence of the average expirate samples The correction for appar is dead space shown in the table is discussed below

TABLE 25

The relation between carbon monoxide uptake as measure by a post dead spac sample and an average sample of the collected expired gas for different tida volumes when the ventilation remained constant normal subject aged 32 (sitting)

Date	Tidal volume (ml)	Ventilation (l/min)	CO uptake as % of inspirate	
			Average post dead space sample	Average expirate sample
December 18 1950	804	11 7	54 3	47 9 (41 3)
	1 563	11 8	55 3	54 9 (51 1)
December 19 1950	803	11 9	55 7	36 6 (31 6)
	1 590	11 1	57 0	51 6 (52 3)

The figures for the average expirate sample uncorrected for the dead space of the apparatus are given in parentheses

From these results it might be supposed that the absolute CO-dead space (that part of the upper respiratory dead space before absorption takes place) is approximately constant Further, if the sample we obtained was really ... and

gate this, a comparison of the average post dead space ... samples was made in replicate runs on seven other subjects five of whom had ... and whose tidal volumes varied between ... tive tidal ... with the ... 67 From ... umes the ... ure is the ... zero and extrapolation to the tidal volume when the ... no absorption takes place Since however, the open-circuit apparatus itself

had a dead space of about 100 ml , the volume of the upper respiratory tract, dead to carbon monoxide absorption, is estimated at about 80 ml

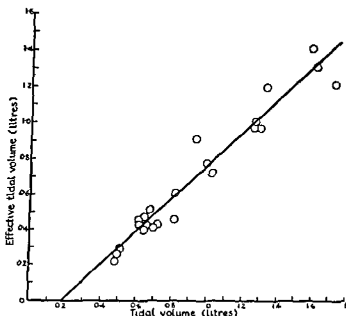


FIG 67 Scatter diagram relating the effective tidal volume required to account for the difference between the average *post dead-space and average expirate samples* of carbon monoxide to the observed tidal volume The line is the linear regression *relating the two variables* E T V = 958 × T V −184

The absolute non absorbing space for carbon monoxide was also investigated by direct experiment in four normal subjects The method adopted was for the subject to place his mouth at one end of the inlet to the actual analysis tube of the infra red gas analyser so that the dead space between him and the analysed gas was only about 5 ml He inhaled a volume of about 1500 ml of 0 3 per cent carbon monoxide mixture through the analysis tube so that the needle of the analyser recorded a steady full scale deflexion, the times of ... He held this volume of carbon monoxide in

from a soap-bubble flowmeter ...
The results are given in Table 26 from which it will be seen that the estimate of the carbon monoxide dead space was the same (79 5 ml) as that derived from Fig 67, and was practically independent of the time of retaining the carbon monoxide mixture

TABLE 26

[illegible] n

T_s = time of inhalation T_1 = time of breath holding, T_2 = time from start of [illegible] until change in the reading of the infra red gas analyser

Subject	Measurement no	Volume (ml)	Ts (sec)	T_1 (sec)	T_2 (sec)
1	1 2 3	76 94 78	10 15 15	2 2 15	7 11 20
2	1 2 3 4 5	75 78 75 70 56	12 12 12 13 12	6 3 2 5 20 20	15 8 9 22 32
3	1 2 3 4 5	75 80 78 78 76	10 10 10 10 10	5 10 2 5 15 2	15 14 7 24 7
4	1 2 3 4 5 6	80 85 82 90 90 95	8 8 8 11 10 10	4 5 1 10 10 4	7 15 3 13 13 6
Mean volume		79 5			

This method of measuring the dead space is technically imperfect since it could not be maintained that the volume of expirate at which a *change* was first noted on our gas analyser is equivalent to the dead space * Inspection of Fowler's curves for nitrogen using the Lilly nitrogen meter shows that the concentration starts to change after about 80 ml

[illegible] seemed probable that the dead space for carbon monoxide is not [illegible] so far examined, and it is likely that [illegible] in Fig 67 is an expression of the [illegible] space sample from a true average [illegible] e) part of the expirate There is, however, little doubt that [illegible] bon monoxide uptake were relatively unaffected by variations in tidal volume

* [illegible] S Fowler for pointing out this error in our method

B THE DIFFUSING CAPACITY OF THE LUNGS*

Having established that our results were not dependent on any of the factors listed by Forbes and others, and that they were not appreciably influenced by the dead space, are we to believe that they are a measure of the diffusion constant of the lung?

This 'diffusion constant' was first defined by Bohr (1909) as the volume of carbon monoxide at N T P removed by the lung in unit time when the difference between the partial pressure on the two sides of the lung membrane is 1 mm Hg Marie Krogh (1915) estimated its value for carbon monoxide when a subject inhaled a large volume of carbon monoxide mixture (1 per cent in air) and held his breath for some seconds, the concentration of carbon monoxide in a small volume of expirate was then determined after about half the lungs were emptied and in a similar sample 0 1 minutes later, the volume of carbon monoxide taken up during the short time interval was found from these samples of expired gas, the volume of which was recorded on a spirometer Assuming a zero back-tension, the diffusion constant (Dco) was calculated knowing the barometric pressure and estimating the alveolar tension from the samples

Forbes and others (1945) related their results for the uptake of carbon monoxide to the 'diffusion constant' by using the following equation

CO uptake (ml /min) = Dco × CO in alveolar air (%) × P − 47 (mm Hg)

There seems no doubt that, in any such measurement of the 'diffusion constant' for carbon monoxide from the rate of uptake of the gas, what is really measured is a combined function of the true diffusion constant of the membrane and the area of the membrane containing blood which is effectively exposed to the carbon monoxide in the lungs The constant is thus dependent not only on the total alveolar area but also on the ventilation-perfusion ratio in different parts of the lung In other words, it is difficult to distinguish between an increase in the true diffusion constant of the lung membrane and alterations in the ventilation-perfusion ratios in the alveoli caused by shunting of blood or variation in gas-distribution In their effect on the subject the two are identical, a decrease in the overall gas-transfer efficiency occurring with either We shall distinguish between the overall diffusing capacity (Dco) for the lung which was measured by these previous workers and the physical constant for the lung membrane (Kco)

Measurement of Diffusion Constant Kco

There are at least three further difficulties in any attempt to measure the Kco The first is obtaining the area and thickness of the membrane The second is in the assumption that there is no back-tension in the lungs Roughton (1945) suggested that an error of up to 10 per cent may arise in the calculated values

* ... examined the ... it

of the constant on account of local back tension Krogh herself appreciated that this error might exist

The third difficulty, that of estimating the alveolar carbon monoxide tension, is because the tension changes with time In other words the value obtained from a Haldane Priestley sample is a function of the time that elapses before the sample is taken Krogh attempted to evade this difficulty when measuring the constant by taking small samples at known time intervals, Roughton and others by taking alveolar samples in a standard manner and assuming that these bore a constant relation to the average alveolar concentration over the respiratory cycle when using their results for the comparison of one man with another

Comparison with Other Results

We related our values for the proportion of carbon monoxide removed from the inspirate measured by an average post dead space sample to those given for the Dco by Forbes and others in a small confirmatory experiment, using two of our normal subjects and one of the cases of unusual fibrosis who showed extreme impairment of uptake by our test The results are given in Table 27 The effect of the alveolar sample on the value for the Dco when calculated by the method of Forbes and others is also shown

All the alveolar samples in this confirmatory experiment were obtained by the Haldane-Priestley technique at the end of a normal expiration just after the period of carbon monoxide inhalation was completed, all were about 180 ml samples except that taken in the first experiment in the second normal subject, marked with an asterisk in the table this sample was only the last 50 ml of gas (diluted with air to 200 ml for analysis by the infra red gas analyser) The values for the Dco repeated reasonably well both in normal subject No 1 and in the patient No 201 with fibrosis, in whom the value is much lower This abnormality of the Dco value is reflected in the small proportion of carbon monoxide removed from the inspirate as measured by the average post dead space sample Our values for the Dco of the normal subjects agree reasonably with those of Forbes and others, though the importance of the time of sampling the 'alveolar air' is shown in Experiment 1 in Subject No 2 In this instance the value of the Dco calculated from the smaller sample taken lower down the time-concentration curve for carbon monoxide in the expirate, is much higher Forbes and others themselves remarked about their results 'To obtain the 'absolute' values for the diffusion constant the average alveolar carbon monoxide percentage during the respiratory cycle should be used and this, being higher than the expiratory alveolar percentage would lead to lower values (for) • the diffusion constant '

It is evident, therefore, that by this method of calculating the diffusion constant, absolute values are dependent on the particular alveolar sample, but if the alveolar sampling is constant relative to the time of expiration useful comparative measures may be obtained for differences in the overall gas-transfer efficiency of the lungs between one subject and another However, as seen from Table 27, similar comparative measurements to those for diffusing capacity are obtained from the percentage of the inspired carbon monoxide removed, when this is expressed from the average post dead space sample The proportionate change in the abnormal subject with fibrosis is then in fact somewhat greater

TABLE 27

The diffusing capacity of the lung for carbon monoxide for two normal subjects and one subject with pulmonary fibrosis compared with the results reported by Forbes and others (1945)

Measurement	Normal subject No 1 (age 38)		Normal subject No 2 (age 36)		Subject No 201 Pulmonary fibrosis (age 37)		Two normal subjects J F and F C (Forbes and others, 1945)	
	Exp 1	Exp 2	Exp 1	Exp 2	Exp 1	Exp 2		
CO in inspired air (%)	0·3	0·3	0·3	0·3	0·3	0·3	0·259	0·302
CO in expired air (%) (average expirate sample)	0·138	0·162	0·126	0·143	0·165	0·192	0·106	0·102
CO in alveolar air (%)	0·087	0·093	0·03*	0·060	*0·189*	*0·180*	0·035	0·042
Ventilation	13·3	12·8	7·8	9·4	18·9	17·5	5·17	5·83
Dco (ml /unit tension difference)	34·6	27·1	58	40·5	18·0	16·3	*30·0*	*39·0*
CO removed from inspirate (%) (average post-dead space sample)	58	62	54	56	20	22	—	—

* Small alveolar sample (see text)

Effect of Cardiac Output

Cardiac output may affect the overall gas transfer efficiency, it is interesting to note that in the groups of the expirate concentration for many subjects small sinusoidal variations were seen in the equilibrium level (for example, Fig 11, p 68), which were not to be explained either from electrical artefacts or the effects of variation in breathing or pulse rate We have not investigated the effects of changes in cardiac output on the results of this method, though we think it improbable that the decrease in uptake of carbon monoxide in the groups of advanced pneumoconiosis is due to this cause Subsequent work by Hatch and Cook (1955) suggests that carbon monoxide uptake is almost independent of cardiac output

Summary

We think that the test of measuring with an average post dead space sample the proportion of carbon monoxide removed from the inspirate provides a measure of the overall gas transfer efficiency of the lung This is comparable to the measurement of the effective diffusion constant as done by Forbes and others For our purpose it had the great advantage of not requiring an alveolar sample by the Haldane Priestley method (which gives varying results since the carbon monoxide concentration is changing with time) and which would have been impracticable with the untrained subjects in the main experiment The samples we took automatically gave an average alveolar concentration over a considerable part of the volume time curve for a single expirate starting at a fixed interval after the beginning of expiration The test was a useful comparative measure, little influenced by variations in ventilation and tidal volume, but it cannot differentiate between changes in ventilation perfusion ratios and in the diffusion barrier since the two have the same functional effect

Ideally one would like to know the efficiency of gas transfer in terms of oxygen or carbon dioxide However, no method of estimating the diffusion constants of the lungs for these gases has been devised but that for carbon monoxide bears a known relation to them

4 Interrelationship of Helium and Carbon Monoxide Results

It was concluded in the previous section that the proportion of carbon monoxide removed from an inspired gas mixture is a measurement of the effective gas transfer efficiency of the lungs By relating the open circuit helium and carbon monoxide increment curves, which were recorded concurrently, we hoped to allow for that part of the impaired removal of carbon monoxide which was due solely to ventilatory inequality Such an analysis would show whether the ventilatory inequality, by affecting the ventilation perfusion balance was itself enough to account for the defect in carbon monoxide removal in the late stages of pneumoconiosis (p 119)

In this analysis we shall first examine that part of the carbon monoxide increment curve which precedes the establishment of a constant expirate concentration (usually between breaths 0 and 15), and then study the factors influencing the equilibrium level

Derivation of Equations

Single-chamber model The first part of the carbon monoxide curve, before equilibrium, must represent intrapulmonary gas-distribution and transfer proceeding concurrently To study this, a general equation was derived which would represent the simplest case of a single-chamber model which not only mixed perfectly, but which had a uniformly distributed power of absorbing one constituent of the gas-mixture The chamber was assumed to be ventilated by a repetitive cycle of equal tidal volumes and to have no dead-space

For such a chamber the concentration of absorbable gas (expressed as a fraction of the inspirate concentration), after r breaths is

$$C_r = \frac{1}{1+K_{CO}F/Tf}\{1-q^{r(1+K_{CO}F/Tf)}\} \qquad (16)$$

where F = volume of chamber (equivalent to the functional residual capacity), T = tidal volume, f = 'breathing' rate, and K_{CO} = unit volume of gas absorbed/unit volume of chamber*/unit time/unit pressure difference

Or if $\dot{V}$ is the ventilation rate,

$$C_r = \frac{\dot{V}}{\dot{V}+K_{CO}F}\{1-q^{r(\dot{V}+K_{CO}F)/\dot{V}}\} \qquad (16a)$$

With a gas such as helium, K_{He} is approximately zero, so that equations (16) and (16a) become $C_r = 1-q^r$ which is the 'perfect mixing' equation for an inert, non absorbed gas (Part II, p 72) Thus the helium curve is a special case one limit of a whole family of curves, described by the general equation, the other limit being an infinitely absorbable gas ($K_{CO} = \infty$) when $C_r = 0$ Carbon monoxide lies between these extremes and knowing its absorption coefficient it should, in the postulated simple case, be possible to predict the form of its uptake curve from the helium curve

It will be seen from (16a) that $\dot{V}/(\dot{V}+K_{CO}F)$ is the limiting value of $C_r = \frac{\dot{V}}{\dot{V}+K_{CO}F}\{1-q^{r(\dot{V}+K_{CO}F)/\dot{V}}\}$, for when r is sufficiently large, $q^{r(\dot{V}+K_{CO}F)/\dot{V}}$ becomes negligibly small In practice this is so after about 16 breaths So that the concentration of the expirate at the first equilibrium plateau is

$$C_\infty = \dot{V}/(\dot{V}+K_{CO}F), \qquad (17)$$

or

$$C_\infty = 1/(1+K_{CO}F/\dot{V}) \qquad (17a)$$

Equation (16a) can then be restated

$$C_r = C_\infty(1-q^{r/C_\infty}) = C_\infty\{1-(q^{1/C_\infty})^r\} \qquad (18)$$

From (17)

$$K_{CO} = \frac{\dot{V}}{F}\cdot\frac{1-C_\infty}{C_\infty} \qquad (19)$$

and

$$D_{CO} = \frac{\dot{V}}{P}\cdot\frac{1-C_\infty}{C_\infty} \text{ where P is the barometric pressure,} \qquad (20)$$

* For simplicity volume of chamber is used as a function of wall area of constant thickness

Thus *for carbon monoxide,*

K_{CO} = (Ventilation/unit volume of lung) × (ratio of proportion of inspired carbon monoxide absorbed to proportion rejected at equilibrium),

and

D_{CO} = Total volume of gas absorbed by chamber/unit time/unit of barometric pressure

This is the same equation as that derived by Forbes, Sargent and Roughton (1945)

Chambers in parallel Using these formulae it is possible to calculate the equation for a more complex case, that of the combined expirate concentration of two or more such chambers ventilating independently in parallel Such a system of parallel chambers was postulated for the lung to explain the helium data, but if it exists, inspiration and expiration is through a common duct in the lung, and so the chambers are not strictly parallel, independent and without interaction When the observed helium data were analysed, however, the lung appeared (see p 166) to behave as if it consisted of two volumes F_A and F_B ventilated *independently by two tidal volumes* T_A *and* T_B *respectively the* sum of T_A and T_B being less than the observed tidal volume The lung behaved in fact, like a system of two chambers in parallel plus a Bohr dead space It is possible that sequential ventilation could also produce this result

This distribution of effective tidal volumes T_A and T_B, found by analysis of the helium curves, could be used in calculations from the carbon monoxide data *Where J is the* cutting point of the extrapolated linear portion of the experimental curves (Fig 58, p 167)

$$T_A/(T_A+T_B) = J, \quad T_B/(T_A+T_B) = 1-J,$$

$$q_A = F_A/(F_A+T_A), \quad q_B = F_B/(F_B+T_B),$$

$$C_{A\infty} = V_A/(V_A+K_{CO_A}F_A), \quad C_{B\infty} = V_B/(V_B+K_{CO_B}F_B)$$

Then the mean expirate concentration = $\bar{C}_r$

$$= JC_{A\infty}(1-q_A{}^{r/C_{A\infty}})+(1-J)C_{B\infty}(1-q_B{}^{r/C_{B\infty}}) \qquad (21)$$

$$= JC_{A\infty}+(1-J)C_{B\infty}-JC_{A\infty}q_A{}^{r/C_{A\infty}}-(1-J)C_{B\infty}q_B{}^{r/C_{B\infty}} \qquad (22)$$

From (21) or (22) it follows that the mean expirate concentration at equilibrium is

$$C_\infty = JC_{A\infty}+(1-J)C_{B\infty} \qquad (23)$$

$$= J\dot{V}_A/(\dot{V}_A+K_{CO_A}F_A)+(1-J)\dot{V}_B/(V_B+K_{CO_B}F_B), \qquad (24)$$

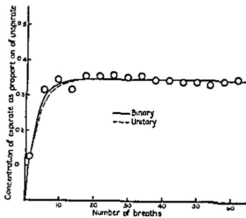
or

$$\bar{C}_\infty = J/(1+K_{CO_A}F_A/V_A)+(1-J)/(1+K_{CO_B}F_B/V_B) \qquad (24a)$$

If an equal diffusion constant for both phases is assumed, that is $K_{CO_A} = K_{CO_B}$, then the overall *K_{CO} may be deduced from the observed mean expirate con*centration* and the volume distributions given by the helium data, using equation (24) In the derivation it is assumed that there is a negligible or constant back-tension of carbon monoxide in the blood (see Appendix III) This $\bar{C}_\infty$ refers to the first equilibrium plateau for carbon monoxide (see Fig 53)

A diffusion constant is, of course, properly measured per unit area of diffusion surface *Our constant is measured per unit volume and we are thus* committed to the assumption that in a particular lung, surface area is

* Forster, Fowler Bates and Van Lingen (1954) have subsequently described the implications of this assumption in detail



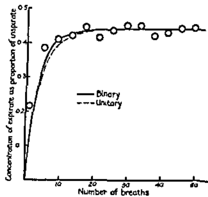


FIG 68b Similar plotting for group N_{55} (10 subjects)

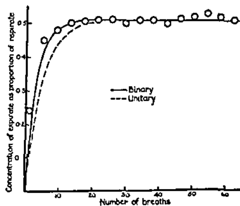
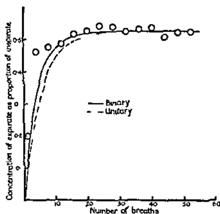


FIG 68c Similar plotting for group D_{55} (8 subjects)



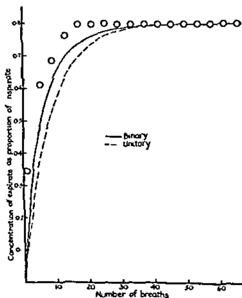


FIG. 69b Similar plotting for Subject No 201 a man aged 32 with an unusual type of pulmonary fibrosis

diffusion imbalance *which is homogeneous in either* phase, which will account for the observed data The distribution of absorptive power would, therefore, appear to be inhomogeneous within each phase, *in which case, with respect* to the absorbable carbon monoxide, the phase behaves as though it were not a perfect-mixing system

Corrections which may be Applied

It is now necessary to see whether the carbon monoxide equilibrium level (usually achieved after about 15 breaths) is influenced by the degree of inequality of ventilation, and also whether it is possible to allow for any alteration caused by *inequality and thus to obtain* an index which is a more valid measure of the impairment of gas transfer

The equation
$$Kco = \frac{V}{F} \frac{1-C_\infty}{C_\infty} \qquad (19)$$

shows how the Kco is related to the equilibrium concentration of a mean expirate (post-dead space) sample and how it allows for variation of ventila

iven Kco
depending
Thus the
bjects will

only remain constant within narrow limits in so far as the ratio F/V for members of that group is similar (assuming they all have the same value for Kco)

A similar dependency exists for a biphasic system but in a more complex fashion, for there is here the complexity that the ratio $F_A/\dot{V}_A$ and F_B/V_B and also $J = T_A/(T_A+T_B)$ may vary with respiratory rate and tidal volume If

have not investigated It requires experi
al and abnormal
e, left with some

uncertainty how to correct for these variables

Table 28 shows that for the means of groups N_{35} and N_{55} the breathing rate f, $F_A/\dot{V}_A$ and $F_B/\dot{V}_B$, and $T_A/(T_A+T_B)$ are fairly constant, so that the observed difference in equilibrium level is possibly accounted for by a real change of Kco which fell from 4 00 to 2 59 In group D_{55} the observed average expirate concentration (Table 28 column 16) was much higher than for the group N_{55} however, the Kco calculated assuming a biphasic system (with equal Kco in both phases) is not much altered from the average *of the normal groups* (column 13) Thus, the greater proportion of carbon monoxide rejected in *each breath in this group would appear* to be the result of the changed mode of ventilation which is reflected by the altered $T_A/(T_A+T_B)$ and $F_B/\dot{V}_B$ ratios, *and the change in* breathing rate

In the emphysema cases (Nos 156 and 158) the Kco is reduced, and in the case of pulmonary fibrosis (No 201) it is much reduced The carbon monoxide uptake is correspondingly reduced Now if the mean Kco *of all the normals* is substituted in the equations appropriate to these cases, a decreased mean

is *predicted* (Table 28, column 17), that is
es would be capable of giving a higher
o were normal The uptake predicted is

much the same as the mean of the cases of advanced pneumoconiosis aged 55, the emphysema cases being a little better, the case of fibrosis slightly worse

Hence, as compared with the normal group, the impairment of carbon monoxide uptake of these cases is apparently due to both ventilatory inequality and reduced Kco It must be emphasized that such conclusions can only be tentative, for it has already been shown that the assumptions made in the calculation of the Kco only apply when there is good agreement between the observed carbon monoxide curve and the one predicted from the helium results using a biphasic scheme There is good agreement in groups N and D, but not in the cases of emphysema and fibrosis

Summary

For the groups of normal subjects and men with advanced pneumoconiosis aged 55, the carbon monoxide results confirm the biphasic hypothesis of gas distribution derived from the helium data This hypothesis, together with the further assumption of an equal diffusion constant per unit volume of lungs (Kco) in both phases, gives the best explanation of the observed carbon monoxide data

The hypothesis breaks down with the emphysema and fibrosis cases, leaving the possibility of a distribution of absorptive power which is non-homogeneous within the phases defined from analysis of the helium results This inhomogeneity might indicate variation in blood distribution within the lung in advanced emphysema, and patchy change in the alveolar-capillary block in the men with unusual fibrosis In pneumoconiosis the difference in carbon monoxide uptake between normal men and men with advanced disease is probably accounted for by inequality of ventilation, the diffusion per unit volume of lung (Kco) being almost the same in the two groups

In emphysema and fibrosis, Kco is reduced, and impairment of carbon monoxide uptake is due both to this and to inequality of ventilation However, as this latter conclusion has been reached by deductions from equations shown to be of doubtful validity it must be treated with reserve

PART IV. INTERRELATION OF THE TESTS BY FACTOR ANALYSIS

ONE of the difficulties of interpreting functional tests in medicine (whether they be of lung, liver or kidney function) is that many are empirical and the extent to which any two tests partly measure the same thing is rarely known But it is desirable, both for reasons of economy of effort and ease of interpretation, to know how much tests overlap Factor analysis of our results by a process of condensation with slight approximation provided a suitable method of seeing this interrelation by enabling the results of all tests to be viewed concurrently using a three-dimensional model Further, our main object was to find the relation of change in lung function to the radiological degree of pneumoconiosis and by introducing age and a numerical scale of radiological abnormality (Table 15, p 126) into the analysis as 'tests', the model provided an excellent summary of the lesion in pneumoconiosis

preliminary analyses included tests thought to be of doubtful value These tests were subsequently discarded if the analysis confirmed this belief The preliminary analysis also confirmed that the addition or subtraction of tests did not affect the interrelation of those remaining

The tests included in the final factor analysis were

Stem height (S H)
Total lung capacity (T L C)

Vital capacity (V C)
Maximum voluntary ventilation (M V V)
Total diaphragm movement (T D M)
Mixing index (I_B)
Mixing index (I_R)
Carbon monoxide uptake (CO)
Age
Radiological category (X ray)

The normal men aged 25 years were excluded from the analysis in order to preserve the balance of the experiment The five cases of advanced emphysema and two of fibrosis were also excluded

A THE TECHNIQUE OF FACTOR ANALYSIS

Stage 1 Calculation of Intercorrelation

The first step was to calculate product moment correlation coefficients between each of the tests in the normal way * The thirteen tests given to each

* The correlation coefficient between two variates x and y is given by the formula —

$$r = \frac{\Sigma[(x-\bar{x})(y-\bar{y})]}{\sqrt{[\Sigma(x-x)^2 \Sigma(y-\bar{y})^2]}}$$

where $\bar{x}$ and $\bar{y}$ are the arithmetic means of the values of x and y respectively The sign Σ indicates summation over all the values in the sample and corresponding values of x and y are used in the product term in the numerator

TABLE 29

Correlation coefficients between each of the thirteen tests

	S H	T L C	F R C	Rd C %	S.V	V C	M V V	T D M	Age	I_B	I_R	CO
T L C	+0·510											
F R.C	+0·325	+0·808										
Rd C %	−0·168	−0·083	+0·389									
S V	−0·143	−0·220	−0·036	+0·329								
V C	+0·522	+0·826	+0·445	−0·533	−0·357							
M V V	+0·317	+0·555	+0·187	−0·582	−0·376	+0·799						
T D M	+0·306	+0·515	+0·144	−0·557	−0·344	+0·744	+0·710					
Age	−0·166	−0·133	+0·047	+0·428	+0·239	−0·338	−0·414	−0·234				
I_B	−0·149	−0·229	−0·002	+0·337	+0·279	−0·403	−0·511	−0·396	+0·203			
I_R	+0·094	+0·301	+0·156	−0·216	−0·239	+0·386	+0·481	+0·382	−0·047	−0·867		
CO	+0·184	+0·251	+0·014	−0·425	−0·300	+0·429	+0·428	+0·400	−0·308	−0·295	+0·259	
X ray	−0·219	−0·555	−0·312	+0·283	+0·406	−0·624	−0·681	−0·575	+0·069	+0·564	−0·740	−0·467

their length That is to say, *on this model the angle between any pair of the* rods (representing tests) shows the extent to which the pair of tests measure the same thing The smaller the angle the more *the tests have in common*, tests at right angles have nothing in common, those projecting in opposite

to construct the model are not shown in Plate 15, for the sake of clarity They are independent reference axes to which the relation of each test is known, *and so once the position of the tests* relative to one another is fixed, their purpose as 'scaffolding' with which to construct the model has been fulfilled and they can be *discarded They would not necessarily be expected to have* any identifiable physiological significance for they were isolated by a technique of analysis which was such that each in turn accounted for the maximum of the remaining covariation of the tests, thus, their choice was simply part of the mathematical procedure

B DESCRIPTION OF THREE-DIMENSIONAL MODEL

Some general aspects of the model will first be described, pointing out examples of how the interrelations shown would be expected from the general

... of necessity constrained
of the model
mitations must

be remembered that the results only represent the attributes of the lungs featuring in our experimental group of subjects, and that the results of tests *represented by short vectors are partially ignored*

An obvious feature in the model is that maximum voluntary ventilation, vital capacity and total diaphragm movement form a group of tests (ringed in Fig 70) presumably measuring the 'bellows action' of the lung Carbon monoxide uptake is also included by this group, but only partially since its rod is much shorter than those of the other tests In the normal subjects this group of tests was negatively related to age (Table 16, p 127), so one would expect to see a similar relation here, *which is apparent in the model as the positive age vector*

... The angle included between age and maximum
ient of correlation of
that given in Table 30,

Total lung capacity and functional residual capacity lie in a general direction approximately at right angles to the 'bellows' group and, therefore, represent

In the normal subjects, vital capacity was the only ...
height (Table 16) and its direction on the model shows the relationship

The mixing indices I_R and I_B are almost perfectly negatively correlated, for they project in opposite directions as would be expected from their mathematical relation (p 168) *They lie in a plane very nearly at right angles to that* including functional residual capacity and maximum voluntary ventilation and, *therefore, mostly measure* yet a third independent factor (this is best seen

in Plate 15) They are, however, partly related to the bellows tests, since they incline (in the horizontal plane of Fig 70) at an angle of about 60° to the bellows group rather than being truly at right-angles Since in normal subjects

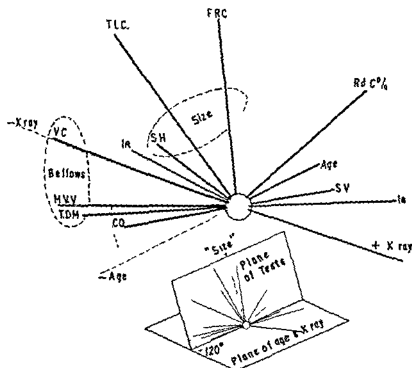


Fig 70 Diagram of the three-dimensional model of the factor analysis showing functional groups formed by the tests Inset shows the relation of the plane of the tests to the 'plane of age and X-ray'

these mixing indices were not related to either age or size (Table 16), their position is what would be expected

Some care is nec[illegible] residual capacity The fact [illegible] is an artificial constraint [illegible] as a percentage, *must be nearly independent of total capacity In other words, the* results of the factor analysis would have been incorrect had residual capacity not either lain at right angles to total lung capacity, which it does, or been of negligible length (communality), which would have implied that total lung capacity itself must be short since residual capacity is part of it If communality were present, residual capacity was only free to rotate in a circle at right angles to total lung capacity The fact that it lay in this plane inclined towards age rather than to the mixing indices is of interest

Age and X ray lie in a plane at about 120° to this 'size' attribute (see inset diagram, Fig 70), this is reasonable because both were only poorly related to height and weight (Table 15, p 126) Age would be expected to be at right-angles to X-ray had the experiment been perfectly balanced, in fact, a low

[illegible]

The reason for the position of the next test, namely carbon monoxide uptake is not immediately obvious and is discussed below

Going on down from axis A on the right hand side, that is in the negative direction, where the measure decreases with increase in ventilatory power, we first pass functional residual capacity near the size axis and there is then a gap to percentage residual capacity It is interesting to find this here, by *standardizing residual capacity for the size of the lung and thus making it at* right angles to total lung capacity, it is forced into this position, which accords with its accepted use as a functional test in that it increases as the overall ventilatory capacity decreases, for example with age, emphysema, etc It does not lie quite in the plane of [illegible] *from the direction seen in F* [illegible] on the axis B, which on th [illegible] would mean that (in so far as it is represented here, for it is a short vector) it is a measure entirely of ventilation which increases as maximum voluntary ventilation, etc decreases This agrees with fact and is the explanation of the sensitivity of the dyspnoeic index

The functional plane The mixing indices I_B and I_R project along the shaded horizontal plane, out of the 'plane of the tests', so it is worth considering what the third dimension indicated by the dotted line C—C in Fig 71, represents Accepting the interpretation of the helium uptake data in Part III (p 168) that I_R and I_B represent the post dead space ventilatory inequality, the obvious suggestion is that it is representing gas distribution Since it is at *right angles to B—B, we must think of it as gas distribution independent* of the degree of ventilation It, too, is a dynamic aspect of the lungs, so the whole plane, B—B C—C will be called the 'plane of function' and is shown diagrammatically in the inset in Fig 71

Change in gas distribution independent of change of ventilation is, however, [illegible] in the lungs, [illegible] inked [illegible] dices, therefore, might be expected to have a component inseparable [illegible] bellows attribute which is concordant with their position between B B and C-C (Fig 71)

The three axes in Fig 71 (inset) are a framework which shows what we believe must be three of the fundamental and independent attributes of the lungs, namely, *static size ventilation ('bellows action') and gas distribution* ('mixing' or ventilatory inequality), which these tests measure in common in a group of men with different radiological degrees of pneumoconiosis

[illegible] of the model in terms of three independent [illegible] f the factor analysis [illegible] ed Their original [illegible]

The Gas transfer Attribute of the Lungs

In the basic three dimensional framework in Fig 71, the known attribute of gas transfer is omitted To understand this, let us consider the carbon monoxide

uptake, which is thought to represent an overall measure of gas transfer, there are two aspects of it in the model first, it is represented by a short vector, secondly, the direction lies close to maximum voluntary ventilation In pneumoconiosis the carbon monoxide uptake is not greatly altered, but, as X-ray

measuring the carbon monoxide uptake is not a useful adjunct to assessment in pneumoconiosis However, in spite of its rather high error the carbon monoxide test has a high specificity, so that, although it changes relatively little in pneumoconiosis, it could be affected in other conditions as the findings in the two cases of unusual pulmonary fibrosis showed

and it seems not unreasonable to suggest that they would then have swung round towards a direction measuring pure transfer

Conclusions

just as the indices I_R and I_B do in the model

To summarize, the importance of appreciating the basic framework is that the farther tests are removed from the static size axis (either by applying the appropriate corrections or, better, by their being pure function measures), the more useful they become Once they are pure measures of function, at least three tests are needed to define fully the performance of the lungs Probably, even if the tests were reduced to three, they would overlap, since it appears unlikely that a test of pure distribution will be devised, because ventilation is tidal and some element of it will be linked to the [illegible]

a

di

the gas-distribution If an effort is made to find a combination of tests with minimum overlap each one does not necessarily measure disability, since they may not be limiting factors It would appear that the best combination is likely to be some measure of maximum ventilatory capacity possibly associated with tests to determine factors such as air-flow resistance and lung viscance which limit the function, together with a test of both non-absorbed and absorbed gas uptake

importance to X ray change in determining disability This becomes at once apparent when one examines a group such as the D_{35}, who, in spite of extreme radiological change, are not nearly as disabled as one might expect from the appearance of their chest radiographs Again, the outstanding feature of pneumoconiosis which we have emphasized is that it adds, as it were, a premium to the changes which occur with age and this is well shown by this analysis

Perpendiculars from the test vectors on to the line B—B (Fig 72) give a good impression of the relative usefulness of the different tests for measuring breathlessness in pneumoconiosis The correlations are not exact since we have no real criterion in the analysis for breathlessness in Fig 72, but the axis is a fair approximation It can be seen at once that functional residual capacity changes* *are of no significance at all, being almost at right angles to B—B* The mixing indices, although so closely related to X ray, have relatively poor significance in disability assessment, like standardized ventilation and carbon monoxide uptake

The 'bellows group are the best tests and are appreciably better than percentage residual capacity All this is consistent with the analysis relating the *tests to clinical grade (p 133) The efficacy of percentage residual capacity,* as a measure of disability, is seen to depend on the fact that it measures almost entirely *the changes which occur in the lung with age, though it has more in* [illegible]

dyspnoeic index is the best measurement of disability in pneumoconiosis

E CONCLUSIONS

A factor analysis of a large body of data like ours provides such a concise summary that it enables other workers to appreciate all the results with a completeness which would otherwise only be possible by lengthy explanation and by separate diagrams By this concise presentation it shows correlations of the tests which would otherwise be missed, and by showing how one test overlaps another, it permits a rational choice of single or multiple tests for any *function of the lungs*

* The size vectors (total lung capacity functional residual capacity) only appear in this projection because the age X ray plane is tilted by the relation of X ray to size In the projection *on to the functional plane they practically disappear*

SUMMARY

Part I

1 Previous work in South Wales has proved that the prolonged inhalation of coal dust alone can cause a disabling form of pneumoconiosis, which differs in its pathological and radiological features from those associated with silicosis (pp 1–3)

2 This coalworkers' pneumoconiosis is not peculiar to South Wales It consists of two distinct pathological processes with characteristic radiographic appearances corresponding to them the first, 'simple pneumoconiosis', results from the retention of coal-dust and increases only if dust exposure continues, the second, 'complicated pneumoconiosis', results from an infective process ('massive fibrosis') superimposed on the simple pneumoconiosis, and, once acquired, may advance independently of any further dust exposure (pp 3–5)

3 Both the clinical features of coalworkers' pneumoconiosis and the interrelation of the many classifications proposed for the various radiographic appearances are summarized (pp 5–12)

4 A review of world literature on previous studies of lung function in pneumoconiosis showed that neither the cause of the breathlessness nor the relation of its severity to the radiographic appearances had been properly established (pp 12–27)

Part II

5 A study of 40 normal subjects and 118 miners between the ages of 23 and 60 years is described The subjects were selected at random and grouped to represent each of four different radiological stages of coalworkers' pneumoconiosis (according to the latest International Classification), so as to complete an orthogonal experimental plan permitting separation of the effects of age and X ray category There were also control groups of non-miners and of working

transfer by a new technique of recording the uptake of helium and carbon

compared well with independent clinical assessment (pp 97–99 and p 133)

(b) The exertional dyspnoea in the coalworkers' pneumoconiosis is mainly caused by a reduction in the maximum ventilatory capacity of the lungs rather

at rest (pp 93–99, 114–124, 136–139)

(c) In general, the relation between the degree of exertional dyspnoea and the radiographic appearance is close if, but only if, age is taken into account Simple pneumoconiosis has a relatively small effect, but does accentuate the

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APPENDIX I

The numbers, ages (to nearest year), radiological code, height (to nearest cm) and weight (to nearest kg) of subjects in the main experiment, according to the plan

Normal

No	Age	X-ray	Ht cm	Stem-ht cm.	Wt kg
[illegible]	28	0—	174	95	63
[illegible]	26	0—	172	90	82
[illegible]	23	0—/	168	87	56
9	24	0—	172	93	70
9	24	0—	164	87	65
2	24	0—	178	91	62
8	27	0—	181	93	81
30	24	0—	180	92	78
15	24	0—	165	88	63
20	24	0—	174	92	66
$\bar{x}$	24.8		172.8	90.8	68
σ	1.6		5.9	2.7	8.8
4	36	0—	171	88	68
5	36	0—/	178	94	69
7	34	0—	184	95	74
31	36	0—	170	91	70
50	34	0—/	164	88	63
53	36	0—/	170	92	59
92	37	0—	181	94	70
94	33	0—	170	89	72
100	35	0—/	183	97	63
110	33	0—/	163	86	48
$\bar{x}$	35.0		171.4	91.4	65.6
σ	1.4		7.6	3.6	7.7
16	45	0—	171	89	82
44	42	0—/	163	87	72
96	46	0—	160	88	52
112	47	0—	171	89	64
119	43	0— /	181	98	66
123	41	0— /	176	94	81
124	43	0— /	174	91	82
137	42	0—	178	92	64
149	45	0— /	171	89	58
159	43	0— /	168	86	57
$\bar{x}$	43.7		171.3	90.3	67.8
σ	1.9		6.5	3.6	11
3	57	0—	177	94	68
17	52	0—/	169	90	60
23	58	0—	161	86	64
33	54	0—	174	92	82
39	55	0—/	177	91	64
42	54	0—	158	84	50
76	54	0—	176	92	71
107	55	0—	158	86	54
108	54	0—	171	89	49
150	55	0— /	175	93	86
$\bar{x}$	54.3		169.6	89.7	65.8
σ	1.7		7.8	3.2	11.8

Normal miner

No	Age	X-ray	Ht cm	Stem-ht cm	Wt kg
57	34	0—	165	90	57
152	36	0—/	152	80	52
157	34	0—/	162	90	55
170	34	0—/	160	84	54
130	36	0—/	168	89	70
151	38	0—/	159	87	50
178	35	0— /	171	90	61
180	37	0—	164	89	66
$\bar{x}$	35.5		162.6	87.4	58.1
σ	1.5		5.9	3.6	7
118	46	0— /	163	89	55
176	43	0—	156	82	54
181	46	0—/	160	86	60
182	47	0—/	171	92	61
147	47	0—/	172	90	62
162	47	0— /	170	91	54
165	41	0—/	171	91	71
192	42	0—	168	89	61
$\bar{x}$	44.1		166.4	88.8	59.6
σ	2.8		6.0	3.3	5
69	56	0—/	175	95	72
103	55	0—	166	88	72
153	55	0—	164	88	72
164	55	0—/	154	82	51
172	56	0—/	167	90	59
132	53	0—	165	89	58
140	50	0—	174	92	60
174	53	0— /	162	90	57
$\bar{x}$	54.0		166.6	89.2	62.6
σ	1.9		6.5	3.7	8

Simple pneumoconiosis — Category 1/2

No	Age	X-ray	Ht cm	Stem ht cm	Wt kg
58	34	2	167	90	61
84	35	2—/	174	90	79
93	36	1 /	166	79	62
101	37	2	162	88	56
126	35	1 /	160	89	61
128	35	2—/	168	89	51
135	36	2—/	162	86	62
184	36	2—	172	94	64
$\bar{x}$	35.4		166.4	88.1	62.0
σ	0.9		5.0	4.3	8.1
59	44	1—	159	86	49
60	46	1	160	84	48
66	46	2—/	170	92	68
95	46	1 /	169	92	69
134	46	2 /	169	91	64
166	45	1—/	163	90	68
171	41	1 /	165	90	58
183	43	1 /	178	92	64
$\bar{x}$	44.6		166.8	89.6	61.0
σ	1.9		6.1	3.0	8
102	55	1 /	161	85	55
139	54	1—	148	86	77
145	54	1 /	169	90	65
167	54	1—	163	85	57
168	53	1—	172	94	72
173	55	1—	165	89	65
179	54	1—/	166	88	60
186	55	2—/	167	89	76
$\bar{x}$	54		165.7	88.3	65
σ	0.7		4.5	3.0	8.5

Simple pneumoconiosis — Category 3

No	Age	X-ray	Ht cm.	Stem ht cm	Wt kg.
15	32	3—/	144	82	46
16	34	3 /	168	89	68
35	37	3 /	170	88	62
37	35	3— /	174	87	66
47	39	3—/	167	87	64
73	39	3—/	166	92	59
117	32	3—/	168	90	67
141	38	3—/	164	78	68
$\bar{x}$	35.6		166.4	86.6	62.5
σ	2.9		5	5.0	7.4
34	43	3—/	161	85	57
42	45	3— /	171	89	68
74	46	3—/	166	88	63
76	42	3—/	166	85	61
77	48	3—/	175	92	83
86	48	4A1/	165	90	67
90	44	3—	161	87	62
194	44	3—/	163	86	59
$\bar{x}$	45.0		166	87.8	65.0
σ	2.2		4.9	2.5	8
24	54	3 /	164	85	59
25	59	4—/	162	85	63
26	56	3—/	158	86	70
27	55	3 /	164	89	65
49	54	3— /	153	81	50
78	53	3—/	171	90	67
83	55	3 /	161	81	57
195	53	3A1/	165	88	61
$\bar{x}$	54.9		162.3	85.6	61.5
σ	2.0		5.3	3.3	6

Complicated pneumoconiosis — Category B

No	Age	X ray	Ht cm.	Stem-ht cm	Wt. kg
10	37	?B5/4	166	89	63
11	37	?B7/5	173	87	58
40	35	3B4 3	174	88	66
85	35	?B4 4	158	86	61
109	36	?A5 6	174	98	83
122	38	3B6/4	175	93	69
138	34	?B5/5	164	86	59
142	37	?B5/5	169	89	57
$\bar{x}$	36.1		169.1	89.5	64.5
σ	1		6.1	4.1	6
12	44	?B5 5	170	83	43
13	43	3B2/3	170	89	53
14	45	?B3/3	170	88	63
38	42	?B6 4	176	93	69
43	47	?B4 5	159	87	46
53	46	?B4 5	167	88	57
129	44	?B3/3	166	88	74
189	41	3B3 5	156	83	48
$\bar{x}$	44.0		164.3	87.4	56.6
σ	2		8.6	3.3	11
21	57	?B4 5	162	86	63
22	57	?B4 5	159	85	59
48	56	?C4 3	167	89	57
51	55	3B3 4	157	82	61
54	51	?B4 4	160	85	56
62	55	?C3 3	163	84	63
72	56	?B5 4	162	88	57
82	54	3B3/3	166	89	69
$\bar{x}$	55.1		162.0	86.0	60.6
σ	1.9		3.4	2.5	4

Complicated pneumoconiosis — Category D

No	Age	X ray	Ht cm.	Stem ht cm	Wt kg
41	37	?D7 5	167	88	53
88	38	?D6/7	171	90	53
89	33	?C5/4	170	93	54
105	37	?C5 5	172	93	72
106	39	?D4 4	173	91	62
187	31	?C4/4	167	88	60
$\bar{x}$	35.5		170	90.5	59.0
σ	3.1		2.4	2.3	7.4
28	44	?D5 5	153	81	41
30	46	?D5 5	155	82	42
46	47	?D4 5	152	86	43
64	43	?C4 5	173	96	74
67	47	?C4 4	167	88	58
79	46	?D4 4	163	89	57
121	45	?D5 4	166	87	52
146	46	?D4/4	165	90	60
$\bar{x}$	45.4		161.8	87.4	53.4
σ	1.4		7	4.7	11.3
18	55	?D4/5	166	87	63
20	60	?D5/4	162	86	61
45	57	?D3/4	151	82	50
98	53	?C4 4	162	89	59
99	56	?D4 5	164	86	55
113	56	?D3/4	174	87	61
114	52	?D5/5	162	87	57
127	51	?D5/4	162	87	51
$\bar{x}$	55		162.9	86.4	57.6
σ	2.9		6.3	2.0	5.3

TABLE IV

The breathing rate, tidal volume and two indices of intrapulmonary gas-replacement, I_0 and N_{90}, measured by closed-circuit spirometry, group means, standard deviation in brackets

Age group	Normal				Normal miner				Pneumoconiosis category															
	Breaths per min.	Tidal volume (ml)	I_0 (per cent)	N_{90}					1/2				3				B				D			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
25	14.6 (4.8)	660 (142)	55.3 (15.9)	20.2 (7.5)																				
35	14.2 (3.3)	756 (256)	53.5 (20.7)	23.0 (15.5)	17.9 (2.6)	595 (129)	46.6 (11.6)	24.8 (6.8)	16.5 (2.3)	659 (106)	44.7 (6.7)	22.7 (8.3)	15.8 (4.2)	634 (106)	45.9 (11.9)	24.8 (17.9)	18.6 (4.8)	620 (111)	39.8 (7.3)	24.5 (6.0)	20.0 (5.8)	599 (40)	34.1 (15.4)	43.4 (37.7)
45	15.4 (4.0)	569 (80)	50.7 (13.2)	25.6 (11.2)	15.6 (3.2)	594 (84)	43.3 (13.9)	29.1 (9.1)	19.3 (3.7)	675 (138)	41.6 (10.7)	27.4 (11.5)	18.9 (3.3)	615 (74)	39.3 (9.3)	28.1 (9.9)	17.9 (3.8)	640 (98)	34.9 (8.4)	28.1 (7.4)	19.7 (4.9)	589 (172)	36.1 (17.0)	39.2 (24.2)
55	12.4 (2.8)	867 (170)	44.3 (11.3)	24.6 (7.3)	16.8 (3.6)	627 (118)	49.1 (16.1)	23.8 (8.0)	15.3 (3.5)	667 (99)	47.9 (13.2)	22.5 (6.7)	20.6 (2.4)	700 (148)	40.2 (12.6)	25.4 (7.7)	20.9 (6.7)	596 (84)	29.5 (11.9)	43.4 (7.9)	19.4 (2.9)	621 (103)	23.8 (8.4)	50.4 (23.2)

Breathing rate and tidal volume are the averages over the first 3 minutes of the part of the spirogram from which the functional residual capacity is calculated

TABLE V

The exercise tolerance test and the maximum voluntary ventilation group means, standard deviation in brackets

Age group	Normal				Normal miner				Pneumoconiosis category 1/2				3				B				D			
	1 Exercise ventilation (l/min)	2 Standardized ventilation (l/min)	3 Maximum voluntary ventilation (l/min)	4 Dyspnoeic index D_I (per cent)	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
25	[illegible]5.2 (5.5)	27.1 (4.1)	150 (17.7)	18 (4.0)																				
35	25.4 (5.2)	26.1 (5.[illegible])	145 (10.0)	19 (4.5)	[illegible]4.6 (1.7)	[illegible]5.9 (3.2)	135 (14.6)	19 (3.7)	24.8 (3.4)	25.1 (2.9)	117 (23.4)	22 (7.6)	30.3 (4.7)	29.1 (4.7)	135 (22.4)	22 (4.0)	[illegible]9.2 (7.8)	30.9 (7.[illegible])	98 (23.8)	34 (12.9)	26.0 (2.1)	30.2 (4.7)	65 (19.8)	50 (17.6)
45	23.6 (3.1)	[illegible]5.1 (2.4)	150 (18.6)	0 (3.7)	6.2 (6.[illegible])	8.1 (8.7)	112 (34.9)	29 (5.6)	[illegible]9.1 (8.2)	32.3 (10.4)	115 ([illegible]6.[illegible])	30 (12.6)	27.0 (4.8)	8.8 (4.8)	101 ([illegible]2.4)	31 (11.3)	29.3 (4.7)	32.9 (7.9)	79 (31.6)	54 (34.0)	[illegible]8.2 (6.3)	35.7 (6.5)	51 ([illegible]3.5)	82 (45.9)
55	[illegible]5.6 (3.3)	27.6 (4.7)	118 ([illegible]7.6)	24 (4.9)	27.1 (4.9)	[illegible]7.6 (5.3)	94 ([illegible]7.7)	33 (4.8)	22.9 (3.9)	[illegible]4.7 (4.4)	100 (43.2)	34 (26.[illegible])	34.6 (7.4)	40.3 (11.8)	81 (21.0)	53 (21.3)	31.9 (5.5)	35.5 (6.3)	61 (7.6)	60 (12.8)	25.7 (4.4)	36.4 (5.5)	33 (10.7)	113 (20.1)

For definition of exercise ventilation and standardized ventilation, see p. 48.
The maximum voluntary ventilation is expressed as the mean of three observations.

TABLE VIII

The total lung capacity and its subdivisions measured by the closed circuit helium dilution method group means standard deviation in brackets

Age group	Normal: Total lung capacity (l)	Normal: Functional residual capacity (l)	Normal: Residual capacity (l)	Normal: Residual capacity (% TLC)	Normal miner				Pneumoconiosis category: 1/2				3				B				D			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
25	6.72 (0.9)	3.31 (0.5)	1.68 (0.3)	25.0 (3.4)																				
35	7.12 (0.9)	3.81 (0.6)	2.05 (0.4)	28.8 (4.4)	6.38 (1.3)	3.59 (0.9)	1.87 (0.8)	28.5 (6.5)	5.79 (0.7)	3.03 (0.4)	1.77 (0.4)	30.5 (6.9)	5.96 (0.9)	3.05 (0.8)	1.80 (0.6)	30.0 (6.1)	5.44 (0.8)	2.73 (0.4)	1.47 (0.2)	27.4 (4.9)	5.28 (1.0)	3.34 (0.6)	2.04 (0.6)	39.0 (8.9)
45	6.97 (0.8)	3.74 (0.8)	2.22 (0.6)	31.6 (5.9)	6.74 (1.4)	3.90 (1.1)	2.46 (0.5)	35.4 (2.7)	6.70 (0.8)	3.64 (0.8)	2.19 (0.7)	34.7 (8.6)	5.88 (1.1)	3.25 (0.7)	2.16 (0.6)	36.8 (8.0)	5.07 (1.2)	2.98 (1.0)	2.00 (0.2)	38.5 (9.5)	4.69 (0.5)	2.93 (0.5)	1.88 (0.4)	40.8 (10.1)
55	6.80 (1.2)	3.92 (0.7)	2.52 (0.6)	37.4 (7.3)	6.14 (0.6)	3.56 (0.7)	2.32 (0.5)	37.6 (7.2)	5.77 (1.2)	3.25 (0.5)	2.17 (0.4)	38.7 (11.0)	5.65 (0.9)	3.31 (0.8)	2.20 (0.6)	38.7 (5.6)	5.04 (0.4)	2.91 (0.5)	1.95 (0.5)	38.3 (7.1)	5.30 (1.3)	3.58 (1.1)	2.41 (1.0)	44.0 (8.0)

TABLE IX

The vital capacity measured by closed circuit spirometry, and the effect of posture on the expiratory capacity group means standard deviation in brackets

Age group	Normal				Normal miner				Pneumoconiosis category															
	Exp a ory capa y (s and ng) (1)	Expira ory capac y (s ng) (1)	E p a o y capac y (ng) (ll)	V al capac y (s ng) (1)					1 2				3				B				D			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
25	1·97 (0·3)	1·62 (0·3)	13 (0·3)	5·04 (0·7)																				
35	·01 (0·4)	1·76 (0·3	1·16 (0·7)	5·05 (0·7)	1·84 (0·4)	1·72 (0·)	·01 (0·2)	4·51 (0·7)	1·41 (0·3)	1· 6 (0·1)	0·70 (0·4)	4·03 (0·6	1·48 (0·1)	1·25 (0·3)	0·82 (0·3)	4·17 (0·6)	1·46 (0·)	1·25 (0·3)	0·88 (0·3)	3·96 (0·3)	1·38 (0·5)	1·22 (0·4)	0·85 (0·3)	3·16 (0·9)
45	1·66 (0·6)	1·52 (0·4)	1·02 (0·3)	4·74 (0·5)	1·67 (0·9)	1·44 (0·3)	0·95 (0·3)	4· 8 (0·6)	1·57 (0·4)	1·46 (0·3)	1·14 (0·4)	4·02 (0·6)	1·44 (0·)	1·'0 (0·5)	0·98 (0·5)	3·72 (0·9)	0·96 (0·5)	0·99 (1·0)	0·57 (0·2)	3·08 (0·7)	0·95 (0·4)	1·05 (0·3)	0·72 (0·4)	2·81 (0·8)
55	1·54 (0·8)	1·39 (0·6)	1·12 (0·7)	4· 6 (0·9)	1· 8 (0·4)	1·37 (0·3)	0·79 (0·3)	3·82 0·9)	1· 7 (0·6)	1·09 (0·5)	0·86 (0·3)	3·61 (1·)	1·09 0·4	1·10 (0·3)	0·74 (0·5)	3·48 (0·6)	1·13 (0·2)	0·96 (0·2)	0·62 (0·2)	3·09 (1·5)	1·07 (0·)	1·17 (0·3)	0·77 (0·4)	2·89 (0·5)

TABLE X

The indices related to inequality of gas-mixing within the lungs measured by open-circuit spirometry, group means, standard deviation in brackets I

Age group	Normal				Pneumoconiosis category																			
	Indices of inequality				Normal miner				1/2				3				B				D			
	Residual index Ir (per cent)	Biphasic index Is (no. of breaths)	N'_{ae}	Effective tidal volume (ml)																				
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
25	87 (6.6)	3.2 (1.1)	21 (5.7)	455 (200)																				
35	85 (5.7)	3.0 (1.1)	23 (6.4)	436 (41)	92 (9.8)	3.6 (2.4)	28 (7.1)	321 (63)	74 (3.8)	6.7 (3.2)	19 (5.0)	450 (160)	79 (10.1)	5.1 (2.3)	20 (3.9)	403 (149)	76 (6.0)	6.0 (1.9)	23 (5.2)	326 (83)	68 (3.7)	7.8 (0.6)	22 (3.2)	429 (144)
45	86 (6.7)	4.7 (2.5)	27 (9.9)	399 (127)	85 (10.9)	4.3 (3.6)	24 (7.7)	421 (63)	75 (6.7)	6.9 (2.6)	28 (6.0)	354 (139)	75 (3.5)	6.7 (1.3)	26 (7.3)	367 (141)	78 (6.8)	5.8 (2.4)	24 (8.1)	346 (82)	69 (5.3)	8.2 (1.1)	23 (5.9)	367 (123)
55	89 (6.9)	4.3 (2.2)	23 (10.9)	484 (186)	88 (8.6)	4.6 (3.5)	28 (12.1)	341 (71)	76 (6.0)	6.1 (1.8)	20 (5.9)	503 (236)	76 (9.3)	6.6 (2.5)	22 (5.5)	421 (128)	75 (9.2)	6.9 (2.4)	24 (5.5)	327 (60)	64 (6.9)	11.8 (4.0)	25 (7.0)	424 (171)

TABLE XI

Measures related to inequality of gas-mixing within the lungs, group means, standard deviation in brackets II

T_A = tidal volume (apparent) of the slow mixing phase
F_A = functional residual capacity of the slow mixing phase (see p 167)

Age group	Normal: 1. T_A (ml)	2. F_A (l)	3. $q_A = \frac{F_A}{F_A + T_A}$	4. $1 - \frac{T_A}{T_B}$
25	324 (121)	2·92 (0·43)	0·90 (0·03)	0·73 (0·09)
35	335 (87)	3·44 (0·59)	0·91 (0·02)	0·77 (0·07)
45	271 (57)	3·31 (0·87)	0·92 (0·02)	0·71 (0·14)
55	315 (75)	3·32 (0·73)	0·91 (0·03)	0·69 (0·14)

Age group	Normal miner 1	Normal miner 2	Normal miner 3	Normal miner 4	Pneumoconiosis category 1/2: 1	1/2: 2	1/2: 3	1/2: 4	3: 1	3: 2	3: 3	3: 4	B: 1	B: 2	B: 3	B: 4	D: 1	D: 2	D: 3	D: 4
35	255 (79)	3·25 (0·86)	0·93 (0·03)	0·79 (0·15)	239 (44)	2·60 (0·15)	0·91 (0·02)	0·54 (0·08)	251 (72)	2·56 (0·64)	0·91 (0·02)	0·64 (0·13)	204 (50)	2·38 (0·40)	0·92 (0·02)	0·63 (0·07)	232 (33)	2·61 (0·61)	0·92 (0·02)	0·54 (0·03)
45	305 (65)	3·52 (1·17)	0·92 (0·03)	0·72 (0·14)	226 (62)	3·25 (0·68)	0·94 (0·01)	0·64 (0·07)	221 (62)	2·85 (0·60)	0·93 (0·02)	0·61 (0·06)	219 (47)	2·63 (0·92)	0·92 (0·04)	0·64 (0·06)	193 (30)	2·51 (0·44)	0·93 (0·02)	0·54 (0·07)
55	257 (74)	3·20 (0·68)	0·92 (0·03)	0·75 (0·08)	281 (111)	2·73 (0·41)	0·91 (0·03)	0·58 (0·07)	245 (52)	2·84 (0·53)	0·92 (0·05)	0·60 (0·09)	193 (25)	2·51 (0·54)	0·93 (0·01)	0·60 (0·08)	198 (75)	2·91 (0·83)	0·94 (0·02)	0·48 (0·08)

TABLE XII

The proportion of carbon monoxide removed from the inspirate measured by open circuit spirometry, group means, standard deviation in brackets

Age group	Normal		Normal miner		Pneumoconiosis category							
	Carbon monoxide uptake (per cent)	Tidal volume (ml)			1/2		3		B		D	
	1	2										
25	66 2 (8 8)	754 (182)	1	2	1	2	1	2	1	2	1	2
35	65 3 (4 6)	716 (40)	63 6 (6 8)	582 (91)	66 0 (6 8)	672 (151)	64 5 (5 1)	651 (113)	59 5 (6 4)	650 (138)	51 2 (8 3)	624 (351)
45	64 9 (5 0)	658 (130)	60 1 (7 2)	679 (114)	66 1 (6 3)	617 (142)	57 6 (3 5)	714 (162)	49 8 (7 0)	659 (95)	53 4 (7 2)	614 (117)
55	55 1 (9 1)	894 (321)	61 3 (6 8)	635 (111)	55 9 (6 1)	819 (372)	60 4 (10 3)	686 (114)	54 6 (11 2)	646 (63)	47 1 (4 9)	593 (113)

TABLE XIII

Subsidiary results on five cases of non industrial emphysema (Nos 154, 156, 158, 175, 177) and another (No 200), and on two cases of pulmonary fibrosis (Nos 201, 202)

Subject No.	Age	X-ray	Height (cm.)	Stem-height (cm.)	Weight (kg.)	Cough	Grade of dyspnoea	Blood pressure	E S R (*mm./hr*)	B R per min.	T V (ml.)	I_e (per cent)	N_4	E V (l./min.)	S V (l min.)	M V V (l./min.)	DL_c (per cent)	Position of diaphragm: Standing: Resting level (cm.)	Standing: *Expiratory level* (cm.)	Standing: Maximum movement (cm.)	Supine: Resting level (*cm.*)	Bronchospasm: History (*per cent*)	Bronchospasm: Examination (*per cent*)
154	56	E	172	92	53	+	*1*	*144/94*	6	16	530	37 2	44	28 4	32 4	50	65	17 3	18 8	2 5	18 0	+	*0*
156	57	E	184	94	61		3	146 86	7	12	900	28 2	32	29 4	30 5	44	69	16 5	19 6	3 2	18 0	+	+
158	58	E	172	88	66	+	4	160/100	12	15	640	38 2	38	21 8	33 1	26	127	13·0	15 3	4 6	16 0	+	+
175	53	E	157	84	49	+	4	142 88	2	16	575		—	21 7	25 2	25	100	10 5	12 3	3 2	11 5	+ +	+
177	38	F	171	89	46	+	3	1.8/78	4	16	530	24 6	73	26 0	32 8	59	55	*12 5*	15 4	4 4	14 3	+ +	0
Mean	*52*		*171*	*89*	*55*				5	15	635	32 0	47	25 5	30 8	*41*	*83*	*13 9*	*16 3*	*4 0*	*15 9*	*70*	*30*
200	12	E	173	84	62		3	130 90	2	17	670	18·0	75	37 0	69 0	41	133			—	—		
201	37	F	163	83	52		3	1.8 85	46	24	600	29 5	44	45 0	76 3	89	86	—	—	—	—		
202	36	F	—	—	88	+	2			9	800	93 5	12	39 5	41 7	84	50	—	—		—		

TABLE XIII (continued)

Subject No	M V V (l/min)	V C (L)	T L C (l)	F R C (L)	Rd C (l)	Rd C. %, T L C	E C (standing) (l)	E C (sitting) (l)	E C (lying) (l)	V C (sitting) (l)	I_R (per cent)	I_B (no of breaths)	N_{ss}	Te (ml)	T_A (ml)	F_A (l)	$q_A = \frac{F_A}{F_A + T_A}$	$J = \frac{T_A}{Te}$	CO uptake (per cent)	T V (ml)
154	34	8	8·09	5·90	4·43	54·8	1·27	1·47	1·26	3·66	61	14	33	508	252	5·00	0·95	0·50	58·2	619
156	55	2	7·53	5·54	3·59	47·7	1·33	1·95	1·08	3·94	43	17	22	791	287	4·66	0·94	0·36	48·2	819
158	15	53	8·88	7·15	6·38	72·0	0·91	0·77	0·69	2·50	48	17	36	556	266	6·07	0·96	0·48	41·2	645
175	20	18	5·87	4·47	3·43	58·5	0·66	1·04	0·57	2·44	59	12	20	688	287	3·88	0·93	0·42	51·5	610
177	2	2	9·30	7·51	5·82	62·6	1·88	1·69	1·49	3·48	57	24	55	404	200	6·74	0·97	0·50	44·9	618
Mean	25	17	7·93	6·11	4·73	59·1	1·21	1·38	1·02	3·20	54	17	33	589	258	5·27	0·95	0·45	48·8	662
200	—	—	6·55	4·78	3·07	46·5	—	1·71	—	3·49	63	18	26	552	244	4·10	0·94	0·44	26·0	—
201	—	—	5·01	3·20	2·07	41·3	—	1·13	—	2·94	86	7	21	406	224	2·57	0·92	0·55	20·5	—
202	—	—	5·66	2·83	1·32	23·3	—	1·51	—	4·34	70	7	16	503	252	2·36	0·90	0·50	25·0	—

APPENDIX II

Medical Histories of the Cases of Non-Industrial Emphysema and Pulmonary Fibrosis

INDIVIDUAL medical histories of the cases of pneumoconiosis are not included because all the essential information is given in Tables I–IV, Appendix I The details of the medical history and the clinical findings for the cases of non-industrial emphysema and pulmonary fibrosis are given below

Subjects Nos 154, 156, 158, 175 and 177 had been attending a special clinic directed by Professor R V. Christie, for the study and treatment of cases of emphysema at St. Bartholomew's Hospital, London The subjects were selected by Professor Christie and Dr J. Knott as being typical of moderately advanced disease, but they were all sufficiently well to make the journey to Cardiff unassisted, and were examined at the same time as the miners in the main experiment.

Subject No 200 also had non industrial emphysema, but on account of the unusual medical history our findings on this man have been separated from the remainder of the group

Subjects Nos 201 and 202 with pulmonary fibrosis were introduced to us by Dr J D Spillane, who had noticed that their chest radiographs resembled simple pneumoconiosis Both men were being treated for diabetes insipidus

CASES OF NON-INDUSTRIAL EMPHYSEMA

[illegible]

... December, 1950, there was no post mortem examination

Subject No 156 *aged* 57 He had been well until the age of 28, when he had an attack of bronchitis in the winter and was in bed for 3 weeks For the next 8 years he had further attacks each winter [illegible]

[illegible]

was now orthopnoeic and had attacks of wheezing and tightness in his chest, especially at night and in cold weather On two occasions in the previous 5 years a small haemoptysis had

the chest

The radiograph showed low flattened diaphragms and horizontal ribs The lung fields were not abnormally translucent but showed little change in density between inspiration and expiration

examination

Subject No 158 aged 58 He had been a clerk all his life except during the First World War

seriously disabled with marked abnormal physical signs in his chest There was no certain clinical evidence of cardiac failure

Subject No 175 aged 54 He had worked as a French polisher all his life, except during the First World War when he was gassed on more than one occasion but never severely enough to be sent to hospital For the last 30 years he had had a morning cough often severe enough

and frequent attacks of asthma and bronchitis,
work and
ages of 26
attacks of
e to work,
e sputum
ng

ich earlier
hildhood
as a clerk

Radiographs showed no obvious abnormality except a very small change in translucency between the inspiratory and expiratory films There was no evidence of pneumoconiosis

evidence of cor pulmonale

Summary

These men have in common a history of cough and increasing shortness of breath, for which no other cause than emphysema could be found The physical signs in the chest were those usually associated with emphysema The variety of the symptoms referable to the chest preceding the onset of breathlessness, and the dissimilarity of the chest radiographs suggest that they do not form a homogeneous group aetiologically, however, at the time we examined them the pattern of functional disturbance was similar Four out of six died within 3 years from the time we investigated them

CASES OF PULMONARY FIBROSIS

Full details of subjects Nos 201 and 202 have been published (Spillane, 1952), subject No 201 being Case 2 and subject No 202 Case 3 in Spillane's paper on "Diabetes Insipidus and Pulmonary Disease" Only a brief summary of the cases is, therefore, given here

Subject No 201 *aged* 37 This man had been well until the age of 30 when he noticed he was short of breath on exertion and easily became tired A chest radiograph showed diffuse mottling Shortly afterwards he developed polyuria and a diagnosis of diabetes insipidus was made This was controlled by Pitressin For the last 3 years he had been getting more short of breath but was otherwise well

Pitressin

[illegible]

"*Discussion*

"The changes in the hypothalamus were considered to be indicative of an eosinophilic type of granuloma of unknown cause but similar to those previously described. The picture in some areas was reminiscent of sarcoidosis

"The lung changes appear compatible with the healing stage of an eosinophilic granuloma

"There were no features in any organ to suggest the syndromes of Hand Schuller Christian or Letterer Siewe's disease which are regarded as related to eosinophilic granuloma"

Summary

These two subjects both had diabetes insipidus and remarkably similar chest radiographs The nature of the generalized pathological process in subject No 202 is uncertain even at autopsy Whether subject No 201 has the same process causing his symptoms is unknown The two cases are included in this report because they exhibit a disturbance of the uptake of carbon monoxide to a degree far exceeding that found in any of the miners even with the most advanced stage of pulmonary fibrosis caused by complicated pneumoconiosis

APPENDIX III

The Derivation of Equations Representing Different Models for Pulmonary Gas-mixing and Uptake

1 THE GENERAL APPROACH

IN many parts of the report, different theoretical models of the lung have been presented to explain and to use the data from serial gas-replacement experiments They are summarized in Part III, p 177 Here we give the derivation of equations which represent curves relating the concentration of gas-mixture to the number of breath-cycles, which would be obtained from such models if observed on either the open- or closed-circuit apparatus The former can be regarded as a special case of the latter in which the machine volume is infinitely great

It is assumed that both the machine and the lung models are 'perfect-mixing' systems, the gas-mixtures in each being of uniform, though not the same, composition at any time during the breathing cycle It is also assumed that when the lung model is a multivolume system in which different proportions of the tidal volume go into two or more volumes in parallel, then each of these parallel volumes will contain gas of uniform composition at the same phase of the breathing cycle

In any model of the lung we visualize the summation of increments of change in concentration occurring at each identical repetition of the breathing cycle Two methods of approach to this concept will be described a specific method, only suitable for dealing with the simple model of the lung as a single chamber, and a more general method, applicable to this simple case and to more complex multiphase models or to models breathing an absorbable gas

Specific Method

In this, it is shown that the ratio of the $(r+1)^{th}$ to the r^{th} increment is a constant, so that the whole series of increments must be in geometric progression Hence their sum (which is the total rise in concentration in the lung or total fall in concentration in the machine) is of the form $A(1-q^r)$, where A is a constant and q the ratio of the increments or 'common ratio' of the geometric progression

General Method

In more complex systems, such as those dealing with absorbable gases, serial mixing spaces or two or more volumes ventilating in parallel, gas concentrations are given by an expression consisting of the sum of a number of simple exponentials, the number of these being related to the complexity of the system

The cases considered in this Appendix are described by the simplest of this family of equations in which

$$C_r = A\alpha^r + B\beta^r, \tag{1}$$

where C_r is the concentration of gas at the end of the r^{th} breath cycle and A and B are constants

Writing equation (1) for any three successive breaths,

$$C_r = A\alpha^r + B\beta^r, \tag{2}$$

$$C_{r+1} = A\alpha^{r+1} + B\beta^{r+1}, \tag{3}$$

$$C_{r+2} = A\alpha^{r+2} + B\beta^{r+2}, \tag{4}$$

from which we can derive

$$C_{r+2}-(\alpha+\beta)\,C_{r+1}+\alpha\beta C_r = 0, \tag{5}$$

the correctness of which can be verified by substituting the values of C_r, C_{r+1}, C_{r+2} from (2), (3) and (4) in (5) which will then reduce back to (1)

So that, if for any system, a relationship can be found of the form

$$C_{r+2}-2MC_{r+1}+NC_r = 0 \quad \text{(M and N are constants)} \tag{6}$$

then it can be seen from (5) that $+2M = \alpha+\beta$ and $N = \alpha\beta$

To separate α and β we consider $-2M$ and N as the coefficients of an auxiliary equation

$$x^2-2Mx+N = 0, \tag{7}$$

so that

$$\alpha = M+\sqrt{M^2-N}, \tag{8a}$$

$$\beta = M-\sqrt{M^2-N} \tag{8b}$$

We will now derive equations for the different theoretical models using these two methods

2 SINGLE-CHAMBER PERFECT-MIXING SYSTEM WITH NON-ABSORBED GAS

*Symbols** F = volume of gas in lung at end of normal expiration
T = tidal volume
d = non mixing (anatomical) dead space (part of lung volume)
Te = effective tidal volume (T−d)
V
l_r
m_r

Closed circuit Apparatus

Specific method of derivation

Concentration in lung after $(r+1)^{th}$ breath =

$$l_{r+1} = \frac{Fl_r+(T-d)m_r}{F+(T-d)} \tag{9}$$

Increment in concentration in lung due to $(r+1)^{th}$ breath =

$$i_{r+1} = l_{r+1}-l_r \tag{10}$$

$$= \frac{T-d}{F+(T-d)}\left[m_r-l_r\right] \tag{11}$$

i e the increment in lung concentration due to a single breath is a fixed proportion of the difference in concentrations in the lung and machine at the beginning of that breath We have now to show that successive differences are also in fixed proportion to each other

* For the sake of brevity in the equations in this Appendix, the symbols are simplified from those given in Table 6 and in the main text They are therefore listed here at the beginning of each section

Concentration in machine after $(r+1)^{th}$ breath

$$= m_{r+1} = [(V-T)m_r + dm_r + (T-d)l_{r+1}]/V \qquad (12)$$

∴ Subtracting equation (9) from (12) and rearranging terms

$$\frac{m_{r+1}-l_{r+1}}{m_r-l_r} = \left[\frac{F}{F+(T-d)}\right]\left[\frac{V-(T-d)}{V}\right] \qquad (13)$$

$$\therefore \frac{l_{r+2}}{l_{r+1}} = \left[\frac{F}{F+(T-d)}\right]\left[\frac{V-(T-d)}{V}\right] = \left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right] = \text{a constant}, \qquad (14)$$

i e the increments in concentration in lung gas due to successive breaths are in the constant ratio

$$\left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]$$

and their sum to r terms

$$= l_r - l_0 = (m_0 - l_0)\frac{V}{F+V}\left\{1-\left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]\right\} \qquad (15)$$

If the concentration of gas in the lung is zero at the start of the experiment ($l_0 = 0$), then the concentration in the lung after r breaths

$$= l_r = m_0\left(\frac{V}{F+V}\right)\left\{1-\left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]^r\right\} \qquad (16)$$

In the symbols of the main text (Table 6) this becomes

$$CE_r = Cm_0\left(\frac{Vm}{F+Vm}\right)\left\{1-(Q)^r\right\} \qquad (17)$$

The drop in concentration in the machine

$$= \frac{l_r F}{V} = m_0 - m_r = m_0\left(\frac{F}{F+V}\right)\left\{1-\left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]^r\right\} \qquad (18)$$

Since

$$\left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]^{\infty} = 0, \qquad (19)$$

then the total fall in concentration in the machine at completion of mixing is

$$m_0 - m_\infty = m_0\left(\frac{F}{F+V}\right) \qquad (20)$$

Dividing equation (18) by (20), the fall in concentration in the machine up to any breath, r, as a fraction of the final fall is

$$\frac{m_0-m_r}{m_0-m_\infty} = 1-\left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]^r \qquad (21)$$

In the symbols of Table 6 equation (21) becomes

$$\frac{Cm_0-Cm_r}{Cm_0-Cm_\infty} = 1-(Q)^r \qquad (22)$$

which, when the effect of dead space is neglected (as in the index I_0), becomes equation (1b) of p 58

General method of derivation

$$l_{r+1} = \left(\frac{F}{F+Te}\right) \; l_r + \left(\frac{Te}{F+Te}\right) \; m_r \tag{23}$$

$$m_{r+1} = \left(\frac{V-Te}{V}\right) \; m_r + \left(\frac{Te}{V}\right) \; l_{r+1} \tag{24}$$

Rearranging (24)

$$\left(\frac{Te}{V}\right) \; l_{r+1} = m_{r+1} - \left(\frac{V-Te}{V}\right) \; m_r \tag{25}$$

$$\left(\frac{Te}{V}\right) \; l_r = m_r - \left(\frac{V-Te}{V}\right) \; m_{r-1} \tag{26}$$

By substitution from (25) and (26) into (23)

$$m_{r+1} - m_r\left\{1 + \left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]\right\} + m_{r-1}\left\{\left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]\right\} = 0 \tag{27}$$

This equation of linear difference has a solution

$$m_r = A\alpha^r + B\beta^r \tag{28}$$

where A and B are constants and α and β the roots of

$$x^2 - \left\{1 + \left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]\right\}x + \left\{\left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]\right\} = 0 \tag{29}$$

$$\alpha = 1$$

$$\beta = \left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]$$

$$m_r = A + B\beta^r \tag{30}$$

Since

$$m_0 = A + B \tag{31}$$

and

$$m_\infty = A \tag{32}$$

$$m_r = m_\infty + (m_0 - m_\infty)\beta^r \tag{33}$$

Total drop in concentration in the machine =

$$m_0 - m_r = (m_0 - m_\infty)\,(1-\beta^r) \tag{34}$$

$$m_\infty = \frac{l_0 F + m_0 V}{F+V} \tag{35}$$

$$m_0 - m_r = (m_0 - l_0)\frac{F}{F+V}\left\{1 - \left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]^r\right\} \tag{36}$$

i when $l_0 = 0$ is

$$m_0 - m_r = m_0\frac{F}{F+V}\left\{1 - \left[\frac{F}{F+Te}\right]\left[\frac{V-Te}{V}\right]^r\right\} \tag{37}$$

Specific Method See equation (18)

Open circuit Apparatus

When a single-chamber model is recorded with an open-circuit apparatus, the case is simplified because the inspirate concentration is constant. This would occur with a closed circuit machine of infinite volume so that the equation for change of gas concentration in the lung can be derived from the corresponding closed-circuit equation by the substitution of $V = \infty$.

Hence from equation (16) when $l_0 = 0$,

$$l_r = m_0\left[1 - \left(\frac{F}{F+Te}\right)^r\right] \tag{38}$$

or if the lung gas concentration is expressed as a fraction of the constant inspired concentration, m_0

$$\frac{l_r}{m_0} = \left[1 - \left(\frac{F}{F+Te}\right)^r\right] \tag{39}$$

In the symbols of the main text (Table 6) if the inspirate concentration is taken as unity,

$$CE_r = \left[1 - \left(\frac{F}{F+Te}\right)^r\right] = 1-(q')^r \tag{40}$$

or, when dead space is neglected $1-q^r$

3 SINGLE CHAMBER PERFECT MIXING SYSTEM WITH ABSORBED GAS

Symbols

To simplify the algebra, the unit of time used in the calculations is the time taken to inspire unit volume. The volumes of inspirate and expirate are assumed to be equal as also are the inspiratory and expiratory flow rates. It is assumed that there is no dead space. The unit of concentration is for pure gas: all concentrations thus lie between unity and zero.

t = units of time or volume
T = tidal volume
$\dot{V}$ = minute volume
y = concentration of gas in chamber
h = concentration of gas inhaled
F = volume of gas in chamber when $t = 0$
k = absorption coefficient
= mass of gas absorbed by chamber/unit time/unit concentration (assuming that the tension gradient across the membrane is numerically equal to the concentration in the chamber, i.e. no back tension)

Note If time is measured in minutes and a diffusion-constant, K_y, is defined such that

K_y = mass of gas absorbed/minute unit volume of lung unit concentration,

then $k = \dfrac{FK_y}{2\dot{V}}$

Analysis of Single Breath-cycle

We are considering a single perfect-mixing chamber absorbing the gas being mixed in proportion to the concentration present It is necessary to find an expression for the concentration in it, at any phase of the breath cycle, before equations applicable to the closed- or open-circuit apparatus can be developed

Inspiratory phase Consider an inspiratory phase when a volume t has been inspired (in time t) A further finite volume Δt is inspired (in time Δt) The concentration in the chamber is now

$$\frac{y(F+t)+h\Delta t-ky\Delta t}{F+t+\Delta t} \tag{41}$$

The increment in concentration =

$$\Delta y=\frac{y(F+t)+h\Delta t-ky\Delta t-y(F+t+\Delta t)}{F+t+\Delta t} \tag{42}$$

$$=\frac{\Delta t(h-y)-ky\Delta t}{F+t+\Delta t} \tag{43}$$

In the limit as $\Delta t \rightarrow 0$

$$\frac{dy}{dt}=\frac{h-y}{F+t}-\frac{ky}{F+t} \tag{44}$$

$$\frac{dy}{h-(1+k)y}=\frac{dt}{F+t} \tag{45}$$

The solution of the above equation is

$$-(1+k)^{-1}\log_e[h-(1+k)y]=\log_e(F+t)+\log C \tag{46}$$

$\log_e[h-(1+k)y]=\log_e P(F+t)^{-(1+k)}$ where P is an arbitrary [constant,

$$y=(1+k)^{-1}[h-P(F+t)^{-(1+k)}] \tag{47}$$

If y_0 = concentration of gas in lung when t = 0,

$$y_0=(1+k)^{-1}[h-P(F)^{-(1+k)}], \tag{48}$$

$$P=F^{(1+k)}[h-(1+k)y_0] \tag{49}$$

When t = T (end of inspiration),

$$y_T=(1+k)^{-1}\left[h-\left(\frac{F}{F+T}\right)^{1+k}\left\{h-(1+k)y_0\right\}\right] \tag{50}$$

$$=h(1+k)^{-1}\left[1-\left(\frac{F}{F+T}\right)^{1+k}+y_0\left(\frac{1+k}{h}\right)\left(\frac{F}{F+T}\right)^{1+k}\right] \tag{51}$$

Expiratory phase

$$\frac{dy}{y}=\frac{-kdt}{(F+T)-t} \tag{52}$$

$$\therefore \quad \log_e y=\log_e A[(F+T)-t]^k \quad \text{(A is a constant)}, \tag{53}$$

$$y=A[(F+T)-t]^k \tag{54}$$

When $t = 0$, $y = y_T$ (t being now measured from the beginning of expiration)

$\therefore$ from equation (54), $A = y_T(F+T)^{-k}$ (55)

If y'_t = concentration of gas in lung after a time t from the beginning of expiration,

$$y'_t = y_T(F+T)^{-k}\,[(F+T)-t]^k \tag{56}$$

When $t = T$ (end of expiration),

$$y'_T = y_T\left(\frac{F}{F+T}\right)^k \tag{57}$$

i.e. concentration of gas in lung at the end of an expiration =

$\left(\frac{F}{F+T}\right)^k \times$ [concentration at the beginning of the expiration]

Mass of gas expired (M)

$$\frac{dM}{dt} = y_T(F+T)^{-k}[(F+T)-t]^k \tag{58}$$

$$\therefore\quad M = y_T(F+T)^{-k}\int_T^0 [(F+T)-t]^k \tag{59}$$

$$= -y_T(F+T)^{-k}\,[(1+k)^{-1}\{(F+T)-t\}^{1+k}]_T^0 \tag{60}$$

$$= y_T(1+k)^{-1}\left[(F+T)-F\left(\frac{F}{F+T}\right)^k\right] \tag{61}$$

Mean expirate concentration (C_n)

$$C_n = M/T = y_T(1+k)^{-1}\left[\frac{F+T}{T}-\frac{F}{T}\left(\frac{F}{F+T}\right)^k\right] \tag{62}$$

$$= y_T(1+k)^{-1}\left\{\frac{1-\left(\frac{F}{F+T}\right)^{1+k}}{1-\left(\frac{F}{F+T}\right)}\right\} \tag{63}$$

We shall now apply these relationships to an open- and closed-circuit system

Closed circuit Apparatus

Symbols

m_r = concentration in machine after r^{th} expiration
i_r = concentration in lung after r^{th} inspiration
e_r = concentration in lung after r^{th} expiration
M_r = mass of (absorbable) gas expired into machine during r^{th} expiration

$$i_{r+1} = \frac{m_r}{1+k}\left[1-\left\{1-e_r\left(\frac{1+k}{m_r}\right)\right\}\left(\frac{F}{F+T}\right)^{1+k}\right]$$

$$= \frac{m_r}{1+k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]+e_r\left(\frac{F}{F+T}\right)^{1+k} \quad (64)$$

$$e_{r+1} = i_{r+1}\left(\frac{F}{F+T}\right)^{k} = \frac{m_r}{1+k}\left(\frac{F}{F+T}\right)^{k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]+e_r\left(\frac{F}{F+T}\right)^{1+2k} \quad (65)$$

$$M_{r+1} = \frac{i_{r+1}}{1+k}\left[(F+T)-F\left(\frac{F}{F+T}\right)^{k}\right] \quad (66)$$

Mass of (absorbable) gas in machine after $(r+1)^{th}$ expiration

$$= m_r(V-T)+\frac{i_{r+1}}{1+k}\left[(F+T)-F\left(\frac{F}{F+T}\right)^{k}\right] \quad (67)$$

$$= m_r(V-T)+\frac{m_r(F+T)}{(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2$$

$$+\frac{e_r}{1+k}\left(\frac{F}{F+T}\right)^{1+k}(F+T)\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right] \quad (68)$$

$$\therefore \quad m_{r+1} = m_r\left\{\frac{V-T}{V}+\frac{F+T}{V(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2\right\}$$

$$+\frac{e_r}{V}\frac{(F+T)}{(1+k)}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]\left(\frac{F}{F+T}\right)^{1+k} \quad (69)$$

From (65)

$$e_{r+1}-e_r\left(\frac{F}{F+T}\right)^{1+2k} = \frac{m_r}{1+k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]\left(\frac{F}{F+T}\right)^{k} \quad (70)$$

$$e_{r+2}-e_{r+1}\left(\frac{F}{F+T}\right)^{1+2k} = \frac{m_{r+1}}{1+k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]\left(\frac{F}{F+T}\right)^{k} \quad (71)$$

Substituting in (69) and rearranging, we have

$$e_{r+2}-e_{r+1}\left[\left(\frac{F}{F+T}\right)^{1+2k}+\left\{\frac{V-T}{V}+\frac{F+T}{V(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2\right\}\right]$$

$$+e_r\left(\frac{F}{F+T}\right)^{2k}\left(\frac{V-T}{V}\right)\left(\frac{F}{F+T}\right) = 0 \quad (72)$$

the solution of which is

$e_r = AQ_1^r+BQ_2^r$ where A and B are constants

If (72) is written

$$e_{r+2}-2ae_{r+1}+be_r = 0, \quad (73)$$

then

$$Q_1 = a+\sqrt{a^2-b} \quad (74)$$

and

$$Q_2 = a-\sqrt{a^2-b} \quad (75)$$

A value for A can be found for any arbitrary values of e_0 and m_0, although experimental conditions are usually such that $e_0 = 0$

If $e_0 = 0$, then

$$A+B = 0 \quad (76)$$

The general solution when $e_0 = 0$ is

$$e_r = A(Q_1^r - Q_2^r), \tag{77}$$

$$\therefore \quad e_1 = A(Q_1 - Q_2), \tag{78}$$

$$= \frac{m_0}{1+k}\left(\frac{F}{F+T}\right)^k\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right] \quad \text{(from (65))}, \tag{79}$$

$$\therefore \quad A = \frac{m_0\left(\frac{F}{F+T}\right)^k\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]}{(1+k)(Q_1-Q_2)} \tag{80}$$

Solving for m gives the solution

$$m_r = CQ_1^r + DQ_2^r \tag{81}$$

where C and D are different constants but Q_1 and Q_2 the same exponential coefficients as in the solution for e

When $r = 0$, $\quad m_0 = C + D,$ (82)

so that $\quad m_r = C(Q_1^r - Q_2^r) + m_0 Q_2^r$ (83)

$$\therefore \quad m_1 = C(Q_1 - Q_2) + m_0 Q_2 \tag{84}$$

from (69) $\quad m_1 = m_0\left\{\frac{V-T}{V} + \frac{(F+T)}{V(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2\right\}$ (85)

$$\therefore \quad C = m_0 \frac{\left\{\frac{V-T}{V} + \frac{(F+T)}{V(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2 - Q_2\right\}}{Q_1 - Q_2} \tag{86}$$

Open circuit Apparatus

Here, as in the case of the non-absorbed gas in Section 2

$$V = \infty \quad \text{and} \quad m_0 = 1$$

Hence if

$$Q_1 = \frac{1}{2}\left[1+\left(\frac{F}{F+T}\right)^{1+2k}\right] - \frac{1}{2}\sqrt{\left[1+\left(\frac{F}{F+T}\right)^{1+2k}\right]^2 - 4\left(\frac{F}{F+T}\right)^{1+2k}} \tag{87}$$

$$Q_2 = \frac{1}{2}\left[1+\left(\frac{F}{F+T}\right)^{1+2k}\right] + \frac{1}{2}\sqrt{\left[1+\left(\frac{F}{F+T}\right)^{1+2k}\right]^2 - 4\left(\frac{F}{F+T}\right)^{1+2k}} \tag{88}$$

$$Q_1 = 1, \tag{89}$$

$$Q_2 = \left(\frac{F}{F+T}\right)^{1+2k} \tag{90}$$

$$A = \frac{\left(\frac{F}{F+T}\right)^k\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]}{(1+k)\left[1-\left(\frac{F}{F+T}\right)^{1+2k}\right]} \tag{91}$$

$$\therefore \quad e_r = A\left[1-\left(\frac{F}{F+T}\right)^{(1+2k)r}\right] \tag{92}$$

$$l_{r+1} = \frac{m_r}{1+k}\left[1-\left\{1-e_r\left(\frac{1+k}{m_r}\right)\right\}\left(\frac{F}{F+T}\right)^{1+k}\right]$$

$$= \frac{m_r}{1+k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]+e_r\left(\frac{F}{F+T}\right)^{1+k} \quad (64)$$

$$e_{r+1} = l_{r+1}\left(\frac{F}{F+T}\right)^{k} = \frac{m_r}{1+k}\left(\frac{F}{F+T}\right)^{k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]+e_r\left(\frac{F}{F+T}\right)^{1+2k} \quad (65)$$

$$M_{r+1} = \frac{l_{r+1}}{1+k}\left[(F+T)-F\left(\frac{F}{F+T}\right)^{k}\right] \quad (66)$$

Mass of (absorbable) gas in machine after $(r+1)^{th}$ expiration

$$= m_r(V-T)+\frac{l_{r+1}}{1+k}\left[(F+T)-F\left(\frac{F}{F+T}\right)^{k}\right] \quad (67)$$

$$= m_r(V-T)+\frac{m_r(F+T)}{(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2$$

$$+\frac{e_r}{1+k}\left(\frac{F}{F+T}\right)^{1+k}(F+T)\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right] \quad (68)$$

$$m_{r+1} = m_r\left\{\frac{V-T}{V}+\frac{F+T}{V(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2\right\}$$

$$+\frac{e_r}{V}\frac{(F+T)}{(1+k)}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]\left(\frac{F}{F+T}\right)^{1+k} \quad (69)$$

From (65)

$$e_{r+1}-e_r\left(\frac{F}{F+T}\right)^{1+2k} = \frac{m_r}{1+k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]\left(\frac{F}{F+T}\right)^{k} \quad (70)$$

$$e_{r+2}-e_{r+1}\left(\frac{F}{F+T}\right)^{1+2k} = \frac{m_{r+1}}{1+k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]\left(\frac{F}{F+T}\right)^{k} \quad (71)$$

Substituting in (69) and rearranging we have

$$e_{r+2}-e_{r+1}\left[\left(\frac{F}{F+T}\right)^{1+2k}+\left\{\frac{V-T}{V}+\frac{F+T}{V(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2\right\}\right]$$

$$+e_r\left(\frac{F}{F+T}\right)^{2k}\left(\frac{V-T}{V}\right)\left(\frac{F}{F+T}\right) = 0 \quad (72)$$

the solution of which is

$e_r = AQ_1^r+BQ_2^r$ *where* A and B are constants

If (72) is written

$$e_{r+2}-2ae_{r+1}+be_r = 0, \quad (73)$$

then $Q_1 = a+\sqrt{a^2-b}$ (74)

and $Q_2 = a-\sqrt{a^2-b}$ (75)

A value for A can be found for any arbitrary values of e_0 and m_0, although experimental conditions are usually such that $e_0 = 0$

If $e_0 = 0$, then $A+B = 0$ (76)

The general solution when $e_0 = 0$ is

$$e_r = A(Q_1^r - Q_2^r), \qquad (77)$$

$$e_1 = A(Q_1 - Q_2), \qquad (78)$$

$$= \frac{m_0}{1+k}\left(\frac{F}{F+T}\right)^k\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right] \quad \text{(from (65))}, \qquad (79)$$

$$A = \frac{m_0\left(\frac{F}{F+T}\right)^k\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]}{(1+k)(Q_1-Q_2)} \qquad (80)$$

Solving for m gives the solution

$$m_r = CQ_1^r + DQ_2^r \qquad (81)$$

where C and D are different constants but Q_1 and Q_2 the same exponential coefficients as in the solution for e

When $r = 0$, $\quad m_0 = C+D, \qquad (82)$

so that $\quad m_r = C(Q_1^r - Q_2^r) + m_0 Q_2^r \qquad (83)$

$$m_1 = C(Q_1 - Q_2) + m_0 Q_2 \qquad (84)$$

from (69) $\quad m_1 = m_0\left\{\frac{V-T}{V} + \frac{(F+T)}{V(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2\right\} \qquad (85)$

$$\therefore \quad C = m_0 \frac{\left\{\frac{V-T}{V} + \frac{(F+T)}{V(1+k)^2}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2 - Q_2\right\}}{Q_1 - Q_2} \qquad (86)$$

Open circuit Apparatus

Here, as in the case of the non absorbed gas in Section 2,

$$V = \infty \quad \text{and} \quad m_0 = 1$$

Hence if

$$Q_1 = \frac{1}{2}\left[1+\left(\frac{F}{F+T}\right)^{1+2k}\right] - \frac{1}{2}\sqrt{\left[1+\left(\frac{F}{F+T}\right)^{1+2k}\right]^2 - 4\left(\frac{F}{F+T}\right)^{1+2k}} \qquad (87)$$

$$Q_2 = \frac{1}{2}\left[1+\left(\frac{F}{F+T}\right)^{1+2k}\right] + \frac{1}{2}\sqrt{\left[1+\left(\frac{F}{F+T}\right)^{1+2k}\right]^2 - 4\left(\frac{F}{F+T}\right)^{1+2k}} \qquad (88)$$

$$Q_1 = 1, \qquad (89)$$

$$Q_2 = \left(\frac{F}{F+T}\right)^{1+2k} \qquad (90)$$

$$A = \frac{\left(\frac{F}{F+T}\right)^k\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]}{(1+k)\left[1-\left(\frac{F}{F+T}\right)^{1+2k}\right]} \qquad (91)$$

$$e_r = A\left[1-\left(\frac{F}{F+T}\right)^{(1+2k)r}\right] \qquad (92)$$

From (65) and (66)

$$M_r = e_r \frac{(F+T)}{(1+k)\left(\frac{F}{F+T}\right)^k}\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right] \quad (93)$$

Mean expirate concentration $= E_r$

$$= M_r/T = \frac{e_r\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]}{(1+k)\left(\frac{F}{F+T}\right)^k\left(1-\frac{F}{F+T}\right)} \quad (94)$$

$$= \frac{\left[1-\left(\frac{F}{F+T}\right)^{1+k}\right]^2}{(1+k)^2\left[1-\left(\frac{F}{F+T}\right)^{1+2k}\right]\left[1-\left(\frac{F}{F+T}\right)\right]}\left\{1-\left(\frac{F}{F+T}\right)^{(1+2k)r}\right\} \quad (95)$$

The value of $T/(F+T)$ found in practice is usually sufficiently small for this expression for E_r to simplify to

$$E_r = \left(\frac{1}{1+2k}\right)\left\{1-\left(\frac{F}{F+T}\right)^{(1+2k)r}\right\} \quad (96)$$

but E_∞ = *mean expirate concentration at equilibrium*

$$= \frac{1}{1+2k}$$

$$E_r = E_\infty\left\{1-\left(\frac{F}{F+T}\right)^{(r/E_\infty)}\right\} \quad (97)$$

In the symbols of Table 6

$$\frac{C_{E_r}}{C_{E_\infty}} = 1-(q^{1/C_{E_\infty}})^r \quad (98)$$

The similarity and simple relationship of this equation to the open circuit formula for a non absorbable gas (equation 40) is apparent The equations are identical in form and the exponential coefficient for an absorbable gas is simply that of the non absorbable gas but raised to the power of the reciprocal of the mean expirate concentration at equilibrium In practice, the mean expirate concentration is measured as a fraction of the inspired concentration, thus making the inspired concentration effectively unity

'Diffusion constant' from open circuit data

As stated in the note at the beginning of this section if

K_γ — mass of gas absorbed/minute/unit volume of lung/unit concentration

then $$k = \frac{FK_\gamma}{2V}$$

$$C_{E_\infty} = 1/(1+2k) = V/(V+FK_\gamma) \quad (99)$$

and $$K_\gamma = \frac{V}{F}\left(\frac{1-C_{E_\infty}}{C_{E_\infty}}\right) \quad (100)$$

Relation to Equations for Non absorbed Gas ($k = 0$)

When no absorption takes place C_{E_∞} = inspired concentration = unity

Equation (98) becomes

$$C_{E_r} = 1 - q^r, \tag{101}$$

which is identical with equation (40) when $Cm_0 = 1$, and since $q = q$ when dead space is not considered

These substitutions serve merely to check the not at all obvious correctness of the equations of this section against the simpler equations the correctness of which has been demonstrated by different methods of derivation

4 TWO PERFECT MIXING CHAMBERS IN PARALLEL (BIPHASIC SYSTEM) BOTH FOR ABSORBED AND NON ABSORBED GASES

Symbols

F_A and F_B	= volumes of the two chambers at end of normal expiration
T_A and T_B	= tidal volumes to chambers A and B respectively
K'_A and K''_B	= diffusion constants (K' and K'') pertaining to F_A and F_B respectively, as defined for K_γ at the beginning of Section 3
E_A and E_B	= equilibrium mean expirate concentrations from F_A and F_B respectively
q_A and q_B	= expansion ratios $F_A/(F_A+T_A)$ and $F_B/(F_B+T_B)$ respectively
V_A and V_B	= minute ventilations pertaining to F_A and F_B respectively
J	= $T_A/(T_A+T_B)$
V	= volume of closed circuit apparatus at end of normal expiration
Y_r	= combined mean expirate concentration at r^{th} expiration

Open circuit Apparatus

Absorbed gas Restating equation (97),

$$E_r = E_\infty\left\{1 - \left(\frac{F}{F+T}\right)^{r/E_\infty}\right\}$$

So that

$$Y_r = E_A J\{1 - q_A{}^{(r/E_A)}\} + E_B(1-J)\{1 - q_B{}^{(r/E_B)}\} \tag{102}$$

$$= JE_A + (1-J)E_B \quad \{JE_A q_A{}^{(r/E_A)} + (1-J)E_B q_B{}^{(r/E_B)}\} \tag{103}$$

$$Y_\infty = JE_A + (1-J)E_B \tag{104}$$

Then from equation (99), Y_∞ = observed mean expirate concentration at equilibrium

$$= \frac{J\dot{V}_A}{V_A + F_A K'_A} + \frac{(1-J)V_B}{V_B + F_B K''_B} \tag{105}$$

This equation was used to calculate the diffusing capacity of the lung with the factor of ventilatory inequality removed (see text p 195)

Non absorbed gas The volume components of this equation (105) can be found in the special case when K'_A and $K''_B = 0$, i e when the lung is breathing an inert gas mixture containing, for example, helium

Knowing these, K'_A and K''_B can be found

When $K'_A = K''_B = 0$, $E_A = E_B = 1$ The equation (103) becomes transformed to

$$Y_r = 1-[Jq_A{}^r+(1-J)q_B{}^r] = 1-\left[\frac{T_A}{Te}q_A{}^r+\frac{T_B}{Te}q_B{}^r\right] \tag{106}$$

so that
$$1-Y_r = (T_Aq_A{}^r+T_Bq_B{}^r)/Te \tag{106a}$$

If $q_A > q_B$ then $q_A{}^r$ will become negligibly small compared with $q_B{}^r$ after a certain number of breaths After

Therefore after this point the gra

to a straight line of slope log q_A

Thus J and q_A may be found and hence the other volume components (see text p 172, and Appendix V, p 264)

Closed circuit Apparatus

Symbols

Here certain ratios are represented by specific symbols

T_A/V and $T_B/V = W_A$ and W_B respectively,

$T_A/(F_A+T_A)$ and $T_B/(F_B+T_B) =$ a and b respectively

Increment in concentration in F_A after r^{th} inspiration $= a(m-x)$,
Increment in concentration in F_B after r^{th} inspiration $= b(m-x)$

Mean expirate concentration into machine at r^{th} expiration =

$$E_r - \frac{W_A[x(1-a)+am]+W_B[y(1-b)+bm]}{W_A+W_B} \tag{107}$$

Drop in concentration in machine due to r^{th} respiration =

$$d_r = [(T_A+T_B)(m-E_r)]/V = (W_A+W_B)(m-E_r), \tag{108}$$

$$= W_A(1-a)(m-x)+W_B(1-b)(m-y) \tag{109}$$

Let $(m-x) = u_{r-1}$
and $(m-y) = v_{r-1}$

Then
$$u_r = (1-W_A)(1-a)(u_{r-1})-W_B(1-b)(v_{r-1}), \tag{110}$$

$$v_r = (1-W_B)(1-b)(v_{r-1})-W_A(1-a)(u_{r-1}) \tag{111}$$

If
$$Q_A = (1-W_A)(1-a),$$
$$Q_B = (1-W_B)(1-b),$$
$$R_A = W_A/(1-W_A),$$
$$R_B = W_B/(1-W_B),$$

then

$$u_r = Q_A u_{r-1} - R_B Q_B v_{r-1}, \quad (112)$$
$$v_r = Q_B v_{r-1} - R_A Q_A u_{r-1} \quad (113)$$
$$\therefore \quad u_{r+1} = Q_A u_r - R_B Q_B v_r, \quad (114)$$
$$v_{r+1} = Q_B v_r - R_A Q_A u_r. \quad (115)$$

From which four equations the following two equations of linear difference may be deduced

$$u_{r+1} - (Q_A+Q_B)u_r + Q_A Q_B(1-R_A R_B)u_{r-1} = 0, \quad (116)$$

$$v_{r+1} - (Q_A+Q_B)v_r + Q_A Q_B(1-R_A R_B)v_{r-1} = 0 \quad (117)$$

which have solutions

$$u_r = A\alpha^r + B\beta^r, \quad (118)$$
$$v_r = A'\alpha^r + B'\beta^r, \quad (119)$$

$$\alpha = \tfrac{1}{2}(Q_A+Q_B) + \tfrac{1}{2}([Q_A-Q_B]^2 + 4Q_A Q_B R_A R_B)^{\frac{1}{2}}, \quad (120)$$

$$\beta = \tfrac{1}{2}(Q_A+Q_B) - \tfrac{1}{2}([Q_A-Q_B]^2 + 4Q_A Q_B R_A R_B)^{\frac{1}{2}} \quad (121)$$

Since the analysis of closed-circuit data for the single phase model was in terms of the drop in concentration in the machine we will now develop an equation of this form

From equation (108),

$$d_r = W_A(1-a)u_{r-1} + W_B(1-b)v_{r-1},$$
$$= W_A(1-a)\,[A\alpha^{r-1} + B\beta^{r-1}] + W_B(1-b)\,[A'\alpha^{r-1} + B'\beta^{r-1}] \quad (122)$$

$$\therefore \quad d_r = M\alpha^r + N\beta^r \text{ where M and N are constants} \quad (123)$$

The total drop in concentration in the machine =

$$D_r = d_1 + d_2 + \dots + d_r \quad (124)$$
$$= C(1-\alpha^r) + D(1-\beta^r) \quad (125)$$

$$= (C+D)\left[1 - \left(\frac{C}{C+D}\right)\alpha^r - \left(\frac{D}{C+D}\right)\beta^r\right] \quad \text{(C and D are constants)} \quad (126)$$

If F_A and F_B are at the same concentration at the beginning of the experiment, and the difference between this concentration and that of the machine is taken as unity ($u_0 = v_0 = 1$),

then

$$D_\infty = (C+D) = \frac{F_A+F_B}{F_A+F_B+V} = \frac{F}{F+V} \quad (127)$$

From equation (126), total drop after first breath =

$$D_1 = (C+D)\left[1 - \left(\frac{C}{C+D}\right)\alpha - \left(\frac{D}{C+D}\right)\beta\right] \quad (128)$$

If $(1-a)$ and $(1-b)$ are written q_A and q_B respectively, then from equation (122),

$$D_1 = W_A q_A + W_B q_B \quad (129)$$

From equations (128) and (129) we have

$$\frac{C}{C+D} = \frac{(C+D)(1-\beta) - (W_A q_A + W_B q_B)}{(C+D)(\alpha-\beta)} \quad (130)$$

It should be noted that equation (126),

$$D_r = (C+D)\left[1-\left(\frac{C}{C+D}\right)\alpha^r-\left(\frac{D}{C+D}\right)\beta^r\right]$$

which represents the fall in concentration in a closed-circuit machine due to the ventilation of two volumes in parallel, has the same form as the equation representing the rise in concentration in the lung model of a biphasic system applied to an open circuit apparatus

When $T_A = T_B$ and simultaneously $F_A = F_B$, when any of the components T_A, T_B, F_A or $F_B = 0$ or when $T_A/F_A = T_B/F_B$, then equation (126) becomes identical with that of a single-phase model on the closed circuit apparatus

Although the numerical value of the constants and roots of equation (126) can be obtained graphically, there is no easy way of obtaining the volume components of these constants and roots

5 MIXING CHAMBER WITH SERIAL MIXING SPACE FOR NON-ABSORBED GAS ON OPEN-CIRCUIT APPARATUS

Definition of Serial Mixing Space

The usual single-chamber perfect mixing system envisaged is one in which each element of inspired gas entering the chamber is perfectly mixed with the mixture already present and is retained in the chamber, *which expands to* accommodate the additional volume

A serial mixing space is a non-expanding chamber in which each element of the gas entering mixes with the gas already present and an equal element of the resultant mixture leaves this chamber to pass on into the ordinary expanding chamber Although the simple definition given above has logical difficulties, the system can be exactly described by the differential equation

$$\frac{d\alpha}{dT} = \frac{H-\alpha}{S} \tag{131}$$

where H = concentration *of gas entering the space*,
α
T
S

We will now establish the mean concentration of the gas leaving the serial mixing space

Equation (131) has the solution

$$\alpha_T = H-(H-\alpha_0)e^{\ T/S} \tag{132}$$

$$= H(1-e^{-T/S})+\alpha_0 e^{-T/S} \tag{133}$$

Mass of gas originally present in chamber $= S\alpha_0$, (134)

Mass of gas passing into the chamber $= TH$, (135)

Mass of gas remaining in the chamber $= S\alpha_T$ (136)

Mass of gas leaving chamber $= S\alpha_0+TH-S\alpha_T$ (137)

∴ Mean concentration of gas leaving the serial mixing space
= mean expirate concentration,

$$= H-\frac{S}{T}(H-\alpha_0)\,(1-e^{-T/S}) \qquad (138)$$

Mixing Chamber with Serial Space (Open circuit)

Symbols

S = volume of serial mixing space,
F = volume of expanding mixing space,
T = tidal volume,
k = T/S,
Y_r = concentration in S after r^{th} expiration,
F_r = concentration in F after r^{th} expiration,
y_r = concentration in S after r^{th} inspiration,
H = concentration inspired

$$y_{r+1} = H-(H-Y_r)e^{-k}, \qquad (139)$$

$$F_{r+1} = \frac{FF_r+HT-S(H-Y_r)\,(1-e^{-k})}{(F+T)} \qquad (140)$$

$$Y_{r+1} = F_{r+1}(1-e^{-k})+y_{r+1}(e^{-k}) \qquad (141)$$

Substituting from (139)

$$Y_{r+1} = F_{r+1}(1-e^{-k})+Y_re^{-2k}+H(1-e^{-k})e^{-k} \qquad (142)$$

From (140)

$$F_{r+1}-F_r = \frac{T}{F+T}(H-F_r)-\frac{S}{F+T}(H-Y_r)\,(1-e^{-k}) \qquad (143)$$

$$(F+T)\,(H-F_{r+1})-F(H-F_r) = S(H-Y_r)\,(1-e^{-k}) \qquad (144)$$

From (142) similarly,

$$(H-Y_{r+1})-e^{-2k}(H-Y_r) = (H-F_{r+1})\,(1-e^{-k}) \qquad (145)$$

Let
$$H-F_r = u_r,$$
and
$$H-Y_r = v_r,$$

then (144) becomes

$$(F+T)u_{r+1}-Fu_r = S(1-e^{-k})v_r \qquad (146)$$

and (145) is

$$v_{r+1}-e^{-2k}v_r = (1-e^{-k})u_{r+1} \qquad (147)$$

$$\therefore\quad (F+T)u_{r+2}-Fu_{r+1} = S(1-e^{-k})v_{r+1} \qquad (148)$$

and

$$v_r-e^{-2k}v_{r-1} = (1-e^{-k})u_r \qquad (149)$$

Eliminating u from (146), (147), (148) and (149)

$$(F+T)v_{r+1}-[(F+T)e^{-2k}+S(1-e^{-k})^2+F]v_r+Fe^{-2k}v_{r-1} = 0 \qquad (150)$$

the solution of which is

$$v_r = (H - Y_r) = A\alpha^r + B\beta^r, \tag{151}$$

where A and B are constants and α and β the roots of

$$(F+T)v^2 - [(F+T)e^{-2k} + S(1-e^{-k})^2 + F]v + Fe^{-2k} = 0 \tag{152}$$

A and B can be found from the above equations by the method already demonstrated in this and previous sections

It can be shown that if $Y_0 = 0$, then

$$A + B = H$$

and
$$A = H\frac{\left\{(1-\beta)-(1-e^{-k})\left[\frac{T-S(1-e^{-k})}{F+T}+e^{-k}\right]\right\}}{(\alpha-\beta)} \tag{153}$$

Solving (146), (147), (148) and (149) for u gives

$$u_r = (H - F_r) = M\alpha^r - N\beta^r \tag{154}$$

and if $F_0 = 0$,
$$M + N = H \tag{155}$$

and
$$M = H\frac{\left[(1-\beta) - \frac{T}{F+T} + S(1-e^{-k})\right]}{(\alpha-\beta)} \tag{156}$$

Mean expirate concentration

From equation (138), if the mean expirate concentration at the r[th] expiration $= E_r$, then

$$E_r = F_r - \frac{1}{k}(1-e^{-k})(F_r - y_r) \tag{157}$$

but from equation (141)

$$F_r - y_r = (F_r - Y_r)/e^{-k} \tag{158}$$

$$E_r = F_r - \frac{(1-e^{-k})}{ke^{-k}}[F_r - Y_r] \tag{159}$$

$$= F_r\left[1 - \frac{(1-e^{-k})}{ke^{-k}}\right] + Y_r\left[\frac{(1-e^{-k})}{ke^{-k}}\right]$$

$$\therefore E_r = [H - (M\alpha^r + N\beta^r)][1 - (1-e^{-k})/ke^{-k}] + [H - (A\alpha^r + B\beta^r)][(1-e^{-k})/ke^{-k}] \tag{160}$$

$$= H - \{[M - (M+A)(1-e^{-k})/ke^{-k}]\alpha^r + [N - (N+B)(1-e^{-k})/ke^{-k}]\beta^r\} \tag{161}$$

Thus the expression for the mean expirate concentration for a mixing chamber with a serial mixing space on the open circuit apparatus is of the same form as that for two mixing chambers in parallel on the open circuit apparatus

APPENDIX IV

The Correction for Valve-box Dead-space of an Open-circuit Apparatus used to Calculate Carbon Monoxide Uptake

THE problem is to calculate the ratio of the mass of gas removed by a lung to the mass that has passed in and out of it The gas mixture is inspired through a valve-box of known volume, and the volume and concentration of the collected expirate can be measured at any time

The problem is complicated by the fact that when an absorbable gas is being expired the concentration of the expirate is dropping continuously and thus the mean concentration of gas left in the valve-box (of volume d say) is the mean concentration of the last d units of expirate and is not the same as that of the whole expirate

No allowance is made in this calculation for the dead space of the man and gas in the context below means carbon monoxide

Symbols

Tidal volume = T
Volume of valve box = d
Mean concentration of last d units leaving man = C
Concentration inspired is unity
Collection takes place after equilibrium is reached
Initial concentration in collecting spirometer is zero
Mass of gas inspired by man = dC+(T−d)
Mean concentration of gas leaving valve box and therefore collecting spirometer = C_s

$$= \frac{\text{final concentration in spirometer} \times \text{total volume in spirometer}}{(\text{total volume in spirometer}) - (\text{initial volume in spirometer})}$$

Thus the mass of gas leaving valve-box during expiration = TC_s but mass of gas entering valve box during inspiration = T

$$\text{mass of gas absorbed during respiratory cycle} = T(1-C_s)$$

$$\frac{\text{mass of CO absorbed by lung}}{\text{mass of CO inspired into lung}} = \frac{T(1-C_s)}{(T-d)+dC} = \frac{T(1-C_s)}{(T-d)}$$

if dC is sufficiently small to be neglected

A direct experiment in which a series of small syringe samples were taken from *the dead space at the end of any expiration gave a value for dC which* showed that its neglect led to an error of about 2 per cent in the calculated value of percentage CO removed

APPENDIX V

A Method of relating Linear and Semilogarithmic Graphs of Open-circuit Helium data to obtain Mixing Indices

I METHOD OF GRAPHING

THE *expirate concentration*, as a fraction of the inspired concentration, is plotted against the number of breaths using linear co-ordinates The expirate concentration range is therefore 0 to 1 For the calculation of the mixing indices it is then necessary to plot $\log_{10}$ (1 − expirate concentration) against the number of breaths It is anticipated that this graph will become linear when the mean expirate concentration is greater than 0 6

If the available experimental points are so plotted, one may attempt to draw the best fitting straight line through them But on a log plot it is not easy to give proper weight to points deviating from the line chosen Often if this 'best' line is replotted on a linear scale (de log), then the reconstructed curve may clearly be deviating from the original curve on the linear scale

This difficulty may be overcome in the following way Both linear and *log plots are drawn on the same centimetre graph paper, a double ordinate* scale being used a linear scale of 0 to 1 for the primary expirate concentration curve and a linear scale of logarithmic values 0 to −2 for the log plot, the 0 of the log scale starting at the 1 of the primary curve scale and the −2 at the zero of this scale

A rough curve through the primary points is drawn and the number *of breaths for a mean expirate concentration of 0 9 and 0 99 is noted* Log_{10} (1 − 0 9) and (1 − 0 99) are −1 and −2 respectively This provides a guide as to the general position and slope of the linear part of the log plot

The edge of a transparent set square is laid on the graph paper against the position of these two points Readings of other points can then be made from the edge of the set square as if a pencil line were actually drawn The edge of the set square is now moved slightly until the antilogs of a number of convenient check points (see below), read from the edge of the set square give values of (1 − expirate concentration) against their corresponding number of breaths that follow closely the trend of the original experimental points The aim is to find a line, not on the basis of fitting a few points identically, but of best fitting the whole curve from an expirate concentration 0 7 to 0 99

Convenient check points are expirate concentrations of 0 6, 0 8, 0 9, 0 95, 0 99 Log_{10} (1 − 0 6), (1 − 0 8), (1 − 0 9), (1 − 0 95), (1 − 0 99) are −0 4, −0 7, −1 0, −1 7 and −2 0 respectively

To illustrate the technique an example is shown in Fig 73 The curve A (dotted) is a tentative curve thought to fit the experimental points best on the linear scale From the 90 per cent and 99 per cent points of this curve the corresponding dotted line A is the original line [illegible] point of

2 CALCULATION OF I_R AND I_B INDICES

Index I_B

A log plot of (1 − mean expirate concentration) is made in the manner just described, and a line parallel to the linear portion of it is drawn through the origin (i e through the point 0 on the log ordinate scale) This new line will

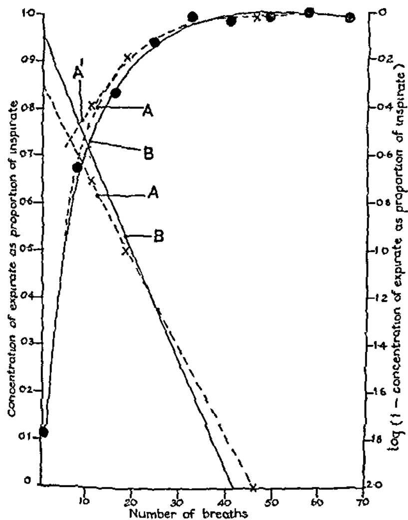


FIG 73 Diagram to illustrate the method of relating linear and semilogarithmic graphs to obtain the indices of gas mixing

APPENDIX V

A Method of relating Linear and Semilogarithmic Graphs of Open-circuit Helium data to obtain Mixing Indices

1 METHOD OF GRAPHING

THE expirate concentration, as a fraction of the inspired concentration is plotted against the number of breaths using linear co ordinates The expirate concentration range is therefore 0 to 1 For the calculation of the mixing indices it is then necessary to plot $\log_{10}$ (1 − expirate concentration) against the number of breaths It is anticipated that this graph will become linear when the mean expirate concentration is greater than 0 6

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This difficulty may be overcome in the following way Both linear and log plots are drawn on the same centimetre graph paper, a double ordinate scale

curve

0 of

the zero of this scale

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per

ine

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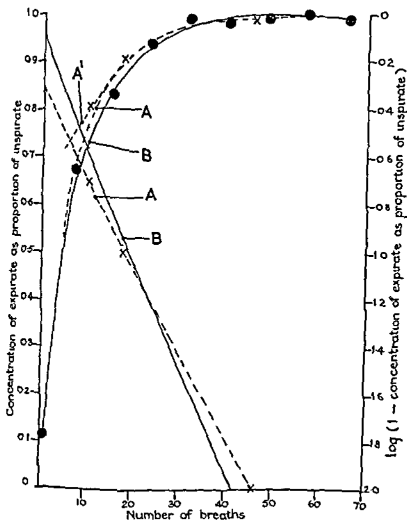


FIG 73 Diagram to illustrate the method of relating linear and semilogarithmic graphs to obtain the indices of gas-mixing

be displaced to the right of the linear portion of the log plot The displacement is measured in units of number of breaths and is the index I_B

The line through the origin represents the concentration changes in the larger mixing space F_A, and so the physical meaning to be attached to I_B is that the concentration of helium in F_A at breath $n+I_B$ equals the mean expirate concentration at breath n The greater the inequality of ventilation of the two components the greater will be I_B

Index I_R

It has already been shown that the acceptance ordinates (1—expirate concentration) represent the uptake of helium by the lung, further, that the sum of all these ordinates equals the functional residual capacity divided by the effective tidal volume

It is more convenient to measure the complete or partial sum of these ordinates by measuring the area above the curve with a planimeter Such areas can be converted into ordinate units by appropriate allowance for the scale of the graph A small error is introduced by equating the area above a continuous curve to the sum of a series of discontinuous operations

Scale Correction

If the total length, in centimetres, of the expirate concentration ordinate scale is, say, 20 cm and the distance, on the breaths scale, between one breath and the next is 0 2 cm , then the equivalent area of one acceptance ordinate is $20 \times 0.2 = 4$ sq cm

The area above the curve in sq cm — 4
= sum of acceptance ordinates = F R C /Te

Derivation of the Index

... mber of breaths is drawn
of breaths
reaths' axis

and cuts the 'mean expirate concentration' axis at unit concentration The total area above the curve bound by the vertical axis and this line is proportional to the total mass of helium finally taken up by the lung This area is measured in sq cm by a planimeter

If the area above the curve between the vertical axis and a vertical line through breath n is measured similarly, then the ratio of this area to the total area is the ratio of the mass of helium accumulated in the lung up to the n^{th} breath to the total helium containing capacity of the lung

To find the index I_R, a value of n is found by trial such that the partial area is 9/10 of the total area

Now, if total area (sq cm)/4 = F/Te, then the

$$\frac{\text{total area}}{4+\text{total area}} = \frac{F/Te}{1+F/Te} = \frac{F}{F+Te} = q'$$

cally) $= N_{90}$, then $I_R = -1/N_{90} \log_{10} q$,

or, expressed as a percentage,

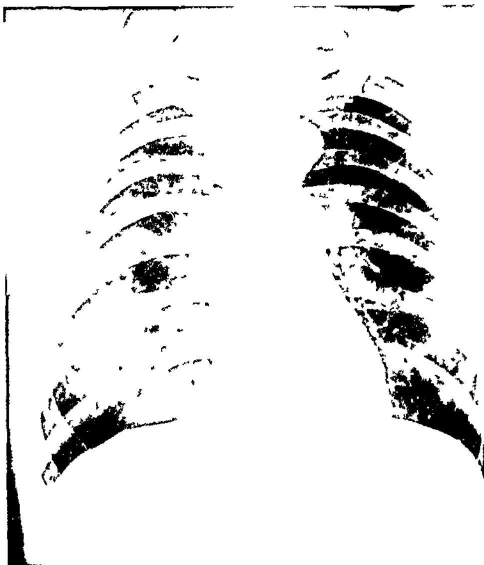
$$I_R = -100/N_{90} \log_{10} q'$$

PLATE 1



Chest rad ograph of normal subject No 33 aged 54 Group N Code O–/

PLATE 3



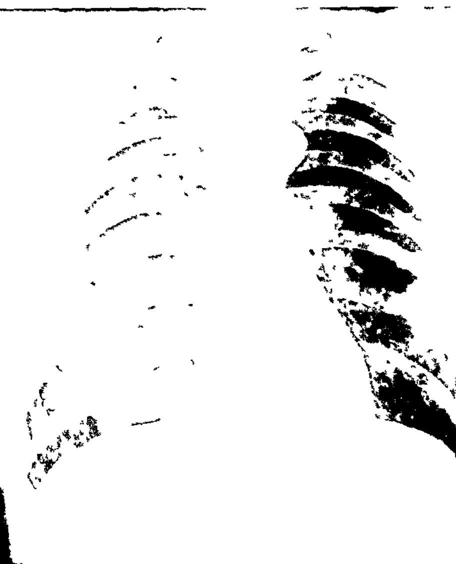
Chest rad ograph of subject No 168 aged 53 with s mple pneumocon os s Group 1/2 Even th s film s abnormal because of the d ffuse granular or nodular appearance wh ch s rather more marked in the r ght lung field than in the left Code 1 /

PLATE 3A



Right m d zone enlarged There is abnormal ty in all rib spaces wh ch conta n fine cities aggregated in some places into larger nodules up to about 5 mm n d ameter g markings partly obscured

PLATE 3



Chest radiograph of subject No. 168 aged 53 with simple pneumoconiosis Group 1 2. Even this film is abnormal because of the diffuse granular or nodular appearance which is rather more marked in the right lung field than in the left. Code 1–/

PLATE 3A



R gh m d zone enlarged There s abnorma y n all r b spaces wh ch conta n fine opac t es aggregated n some places nto larger nodules up to about 5 mm n d ameter Lung mark ngs partly obscured

PLATE 3



Chest radiograph of subject No 168 aged 53 *with simple pneumoconiosis Group 1/2* Even this film is abnormal because of the diffuse granular or nodular appearance which is rather more marked in the right lung field than in the left Code 1--/

PLATE 3A



Right mid zone enlarged. There is abnormality in all rib spaces which contain fine opacities aggregated in some places into larger nodules up to about 5 m
Lung markings partly obscured

PLATE 4



Chest radiograph of subject No 49 aged 54 in the group of simple pneumoconiosis category 3 The diffuse nodular appearance is clearly seen and extends into the outer thirds of both lung fields Code 3–/



Right mid zone enlarged All the rib spaces are almost filled with fine opacities which show more aggregation than in PLATE 3A and also extend in greater profusion into the outer third of the lung field Normal lung markings obscured

PLATE 5



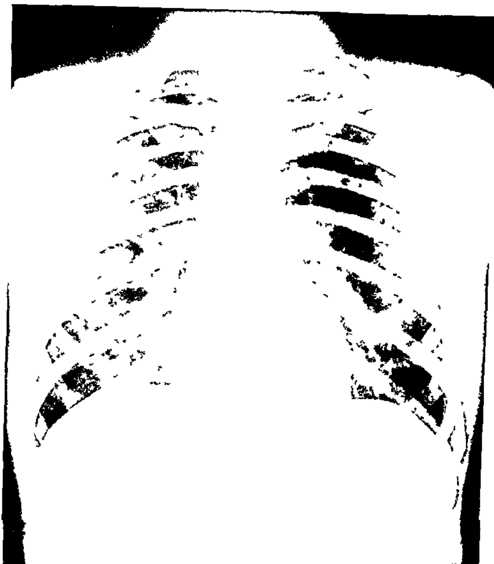
Chest radiograph of miner aged 69 This film is included in category 3 but shows an unusually reticular pattern Normal lung markings replaced by an irregular network of intersecting lines and nodules Code 3 /

PLATE 5A



Right mid zone enlarged. The fine opacities which can still be identified in the background in all rib spaces have aggregated to form nodules which lie in broken chains and so give the whole a reticular appearance. Calcification of the hilar glands is more marked in this film than is common in simple pneumoconiosis in South Wales.

PLATE 6



Chest radiograph of miner aged 25 showing complicated pneumoconiosis category A on a background of simple pneumoconiosis category 2 In the outer third of the second anterior rib space in the right lung field is an indefinite opacity with an irregular hazy outline which merges with the surrounding simple pneumoconiosis Code 2A2/-

PLATE 7



C[illegible] conto[illegible] both [illegible] bases [illegible]

PLATE 8A



k h 0 e 39 n h gro n of compl cated pneumo
I I No 45 except that
I s ncluded to show
re very s m lar to

PLATE 8B



Chest rad ograph of subject No 45 aged 57 in the group of compl cated pn con os s category D The mass e shadows are larger and more homogeneous PLATE 7 and there is d stort on with emphysematous bullae at ap ces The background of s mple pneumocon osis longer vis ble Code "D3/"

PLATE 9A



Chest radiograph of a miner aged 35 with category A complicated pneumoconiosis on a background of category 3 simple pneumoconiosis Code 3A3/0

PLATE 9B





-atus used for measuring maximum voluntary ventilation and vital capacity (open)



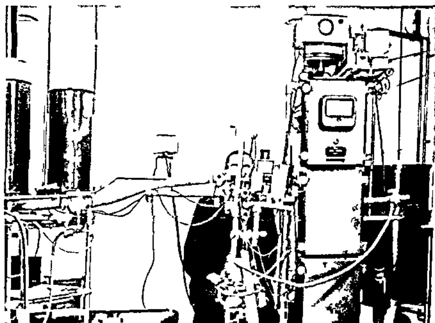
Apparatus used in the standard exercise tolerance test

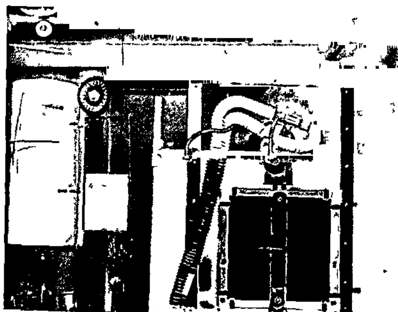
PLATE 12



Closed-circuit spirometer used for measuring the total capacity of the lungs and their gas mixing efficiency

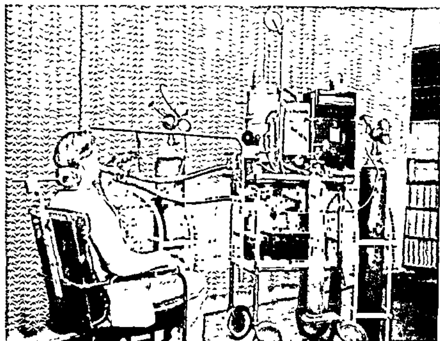
PLATE 13





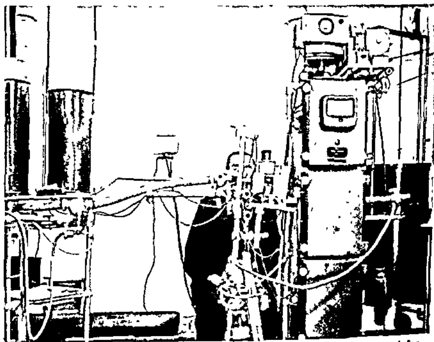
Front view of fluorescent screen with tracking device added for recording diaphragm movement on the kymograph concurrently with spirograph

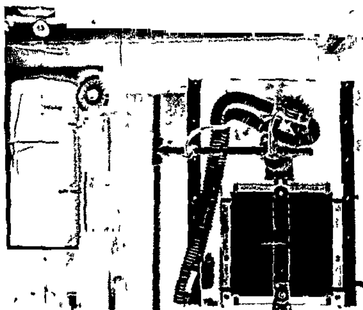
PLATE 12



Closed-circuit spirometer used for measuring the total capacity of the lungs and their gas-mixing efficiency

PLATE 13





Front view of fluorescent screen with tracking device added for recording diaphragm movement on the kymograph concurrently with spirograph